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BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 13 1952

A STUDY OF THE AETIOLOGY OF CARCINOMA OF THE LUNG

BY

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In a previous paper (Doll and Hill, 1950) we reported the first results of a large-scale investigation undertaken to determine whether patients with carcinoma of the lung differed materially from other persons, either in their smoking habits or in some way which might be related to the theory that atmospheric pollution is responsible for the development of the disease. We concluded that smoking is a factor in the production of carcinoma of the lung, and this conclusion was in conformity with the results of some other investigations. Our first observations were, however, limited to patients drawn mainly from London and the adjacent counties. We have now extended the investigation to other parts of the country and have made more detailed inquiries into smoking habits. Many further patients have been interviewed (during January, 1950, to February, 1952) in hospitals in Bristol, Cambridge, Leeds, and Newcastle-upon-Tyne, and also in eight of the twenty London hospitals which co-operated in the first part of the inquiry.

Method of the Investigation

The method of inquiry was described in detail in the previous paper. In brief, we obtained notifications of patients admitted with cancer of the lung, stomach, or large bowel to each co-operating hospital, and these patients were interviewed by almoners, engaged wholly on our research, who recorded the answers to a prearranged questionary. The patients with carcinoma of the stomach or large bowel provided one "control" group, but another, and more important, "control" was obtained by interviewing patients with diseases other than cancer. Each of these latter patients was chosen so as to match a lung-carcinoma patient—namely, of the same sex, within the same five-year age group, and in the same hospital as nearly as possible at the same time.

In the extension of the inquiry this same method has been used, but with modifications. First, notifications were made of patients with lung cancer but no longer of those with cancer of the stomach or large bowel. Secondly, the interviewers could not visit hospitals outside London whenever a suitable patient was admitted; they therefore visited the provincial centres at intervals and interviewed those patients suspected of having lung cancer who were then in the hospitals. At Bristol, Cambridge, and Leeds they also interviewed a few who were attending the outpatient departments.

An important modification was in the choice of the matched control patients. It was impossible to obtain at the provincial centres a group confined, as before, to patients with diseases other than cancer. Our previous analysis, however, had shown that patients with cancer other than lung carcinoma (mainly patients with carcinoma of the stomach or large bowel) gave smoking histories indistinguishable from those given by non-cancer patients; we therefore widened the matched control group to include, with certain exceptions, other forms of cancer. The exceptions which we continued to exclude were cancer of the lip, tongue, mouth, pharynx, nose, larynx, and oesophagus, since it has at times been suggested that cancer of these sites may also bear some relationship to tobacco consumption. We also excluded all other cancers arising inside the chest.

Even then it was still difficult in the provincial centres to find an adequately "matched" control for each lung-carcinoma patient. The provincial hospitals had been chosen so that a large number of lung-cancer patients could be interviewed at each visit. They were therefore thoracic or radiotherapeutic centres serving regions—that is, town and country. We could not seek control patients in the adjacent general hospitals, since these mainly serve the towns they are situated in, and smoking habits vary between town and countryside. On consideration the field of choice was finally extended to other hospitals or units in the same area, but *only* to those serving as regional centres—that is, like the thoracic or radiotherapeutic centres. Thus the cases and their controls should be drawn from equally wide areas of town and country. We have also included in the control series some patients interviewed as having lung cancer but in whom the condition was finally excluded (as at the Brompton and Harefield hospitals in the first part of the investigation). It will be shown that this procedure does not influence the results.

The classification of each patient was, as a general rule, based upon the hospital discharge diagnosis, obtained from a study of the hospital records after the patient's discharge or death. Where that record was indefinite information was obtained from the practitioner or hospital to whose care the patient had been transferred. Occasionally evidence contradicting the hospital discharge diagnosis became available—for ex-

ample, by histological examination at necropsy—and in these cases the diagnosis was based upon the best evidence. Five cases with no record of any final diagnosis have been excluded.

The Data

Between April, 1948, and February, 1952 (the whole period of this investigation), 3,446 cancer patients were notified (lung, stomach, and large bowel). Of these, 156 were aged 75 years or more and were not interviewed, since we limited the inquiry to younger patients who could give more reliable histories of smoking and other personal characteristics. In 82 cases the diagnosis was changed before the almoner paid her visit. Of the remaining 3,208 patients, 85% were interviewed and 498 (15%) were not. The reasons why patients were not interviewed were: already discharged from hospital, 213; too ill, 165; dead, 72; too deaf, 33; unable to speak English clearly, 14; while in one case the interview was abandoned because the patient's replies appeared wholly unreliable. No patient refused to be interviewed. With the lung-cancer group alone the proportion not interviewed was also 15%. We can see no reason why failure to interview all the patients should have biased the results, since it was mainly due to the time that had to elapse between the date of notification and the date of the almoner's visit. Such losses were, of course, few in the provincial centres, since here the almoner was required to interview only those in the hospital at the time of her visit.

The remaining 2,710 patients initially presumed to be suffering from cancer of the lung, stomach, or large bowel and the 1,632 general medical and surgical patients interviewed as matched controls to the lung-carcinoma patients form the subjects of this analysis. Table I gives the numbers in each disease group (final classifications based on the hospital discharge diagnosis, etc., as described above). The 1,488 cases of carcinoma of the lung include 23 for which matched controls had not been interviewed when the investigation ended. Most of our results therefore relate to the 1,465 cases paired with the 1,465 matched controls ("other diseases, A").

Cases diagnosed as carcinoma, or cancer, of the lung or bronchus, pleural endothelioma, and alveolar-cell carcinoma of the lung have been included in the "carcinoma of the lung" group. Classification of the diagnoses according to the recommendation of the International Symposium on the Endemiology of Cancer of the Lung (Council for the International Organizations of Medical Sciences, 1952) gave 70% of the first order of reliability (evidence from biopsy of the primary tumour, from operative, bronchoscopic, or radiographic examination of the primary tumour together with cytological examination of the sputum or biopsy of a secondary tumour, or from necropsy), 29% of the second order of reliability (cytological examination of the sputum alone or operative, bronchoscopic, or radiographic examination without biopsy), and only 1% of the third order of reliability (case history and physical examination alone or death certificate).

The 70 cases classified in Table I as "carcinoma of other special sites" are all other cancers arising inside the chest (for example, sarcoma of lung and cancer of the mediastinum and of the trachea) and those other cancers of the respiratory passages, buccal cavity, and oesophagus for which a possible relationship with smoking has at times been postulated. The 36 cases of "carcinoma of uncertain primary site" include patients with carcinomatosis and some in whom there was doubt whether the lung growth was primary or secondary.

The 1,278 "other diseases, B" include: (1) patients with carcinoma of the stomach or large bowel interviewed in the earlier part of the investigation as a second control group; (2) patients initially interviewed as having carcinoma of the lung, stomach, or large bowel, but later found to have other diseases; and (3) others interviewed as matched controls and not required when the patients with whom they were paired were found not to have carcinoma of the lung.

TABLE I.—*Numbers of Patients Interviewed in Each Disease Group*

Disease Group	No. of Patients Interviewed
Carcinoma of lung	1,488
,, ,, other special sites	70
,, ,, uncertain primary site	36
Other diseases, A (matched controls)	1,465
,, ,, B (other controls)	1,278
Uncertain diagnosis (records untraced)	5
All groups*	4,342

* A further 531 patients were interviewed in rural hospitals, with regard to smoking habits in country areas—see section on estimated risks in town and country.

In Table II the matched patients in the lung-carcinoma and control groups are compared for sex and age distribution, places of interview, places of residence, and, for males, social status. The method of selecting control patients leads automatically to an exact correspondence in sex, age, and places of interview. Differences in social status show no regular trend and are no greater than might be due to chance ($\chi^2=5.28$, n=4, $0.20<P<0.30$). On the other hand, the places of residence reveal considerable differences: fewer of the lung-carcinoma group were residents of Greater London ($\chi^2=17.22$, n=4, $P<0.01$). The meaning of this inequality is considered later (section on place of residence). Since our observations show that the consumption of tobacco tends to be greatest in London the inequality will, if anything, have somewhat reduced the contrasts we find between the groups in their smoking habits. In our previous report, however, we showed that the inequality was unlikely to be of importance.

TABLE II.—*Comparison Between Lung-carcinoma Patients and Matched Control Patients with Other Diseases*

Attribute for Comparison	No. of Lung-carcinoma Patients		No. of Control Patients		Attribute for Comparison	No. of Lung-carcinoma Patients, M and F	No. of Control Patients, M and F
	M	F	M	F			
Age:					Place of interview:		
25–	17	3	17	3	Greater London	1,035	1,035
35–	116	15	116	15	Bristol	73	73
45–	493	38	493	38	Cambridge	36	36
55–	545	34	545	34	Leeds	58	58
65–74	186	18	186	18	Newcastle	263	263
All ages	1,357	108	1,357	108	All places	1,465	1,465
Social class (Registrar-General's categories):					Place of residence:		
I	39	—	53	—	Greater London	791	900
II	165	—	172	—	Other county boroughs	225	181
III	750	—	720	—	Other urban districts	275	213
IV	172	—	198	—	Rural districts	155	164
V	231	—	214	—	Abroad	19	7
All social classes	1,357	—	1,357	—	All places	1,465	1,465

Assessment of Smoking Habits

The difficulties of acquiring and assessing accurately a smoking history and the measures taken to overcome them were discussed in our previous paper. It will be sufficient

to repeat here that the patients were asked (*a*) if they had smoked at any period of their lives; (*b*) the ages at which they had started and stopped; (*c*) the amount they were in the habit of smoking before the onset of the illness which had brought them into hospital; (*d*) the main changes in their smoking history and the maximum they had ever been in the habit of smoking; (*e*) the proportions smoked in pipes and cigarettes; and (*f*) whether they inhaled. A test was made of the accuracy of the answers by cross-examining 50 patients again, six months or more after their first interview. While there was, as expected, some variability of reply, we concluded that the data were reliable enough *to indicate general trends and to substantiate material differences between groups.*

Fortunately the difficulties of inquiry have been reduced through the level of taxation remaining almost constant throughout the investigation. National figures show that the total home consumption remained fairly steady—namely, 213.7, 211.5, 213.8, 221.2 million lb. in the four years ending March 31, 1951 (Board of Trade, 1952). (The last major change in the standard rate of duty payable on tobacco was on April 16, 1947, when it rose from 35s. 6d. to 54s. 10d. a lb.; on April 7, 1948, it became 58s. 2d.)

In the latter stages of the inquiry somewhat fuller smoking histories were sought, and the last 557 lung-carcinoma patients (523 men, 34 women) and their matched controls were asked questions on their use of (*a*) different types and brands of tobacco; (*b*) filter-tipped cigarettes; (*c*) cigarette-holders; and (*d*) petrol lighters.

The Amount Smoked

The results of the inquiry provide a number of ways in which the smoking habits of the patients can be categorized and compared. The simplest is the amount smoked immediately before the onset of the illness which brought the patient into hospital. This, however, can be very misleading, since some persons—including heavy smokers—give up smoking periodically, and it would be wrong to classify them as non-smokers merely because they were interviewed during a period of abstention. In Table III, therefore, the comparison is made in a modified form: non-smokers are defined, as in our previous study, as persons who have never consistently smoked as much as one cigarette a day for as long as one year; the smokers are subdivided either according to the amount they were smoking immediately before the onset of their illness or, if they had previously stopped smoking, according to the amount they were smoking before they last gave up. This is described as "the most recent amount smoked."

Table III shows that in both men and women there were fewer non-smokers and considerably more of the heavier

TABLE III.—*Most Recent Amount of Tobacco Smoked Regularly Before the Onset of the Present Illness: Lung-carcinoma Patients and Matched Control Patients with Other Diseases*

Disease Group	No. of Non-smokers	No. Smoking Daily*				
		1 Cig.–	5 Cigs.–	15 Cigs.–	25 Cigs.–	50 Cigs.+
Men:						
1,357 lung-carcinoma patients (99·9%)	7 (0·5%)	49 (3·6%)	516 (38·0%)	445 (32·8%)	299 (22·0%)	41 (3·0%)
1,357 control patients with other diseases (100%)	61 (4·5%)	91 (6·7%)	615 (45·3%)	408 (30·1%)	162 (11·9%)	20 (1·5%)
Women:						
108 lung-carcinoma patients (100%)	40 (37·0%)	14 (13·0%)	30 (27·8%)	12 (11·1%)	12 (11·1%)	0
108 control patients with other diseases (100%)	59 (54·6%)	18 (16·7%)	22 (20·4%)	8 (7·4%)	1 (0·9%)	0

Difference between proportions of non-smokers and smokers—Men: $\chi^2=43{\cdot}99$, n=1, P<0·000001. Women: $\chi^2=6{\cdot}73$, n=1, P<0·01.
Difference between proportions of smokers smoking different amounts—Men: $\chi^2=69{\cdot}74$, n=4, P<0·000001. Women: $\chi^2=8{\cdot}99$, n=3, 0·02<P<0·05.

* Ounces of tobacco have been expressed as being equivalent to so many cigarettes. There is 1 oz. of tobacco in 26·5 normal-size cigarettes, so that the conversion factor has been taken as: 1 oz. of tobacco a week=4 cigarettes a day.

TABLE IV.—*Most Recent Amount of Tobacco Smoked Regularly Before the Onset of the Present Illness: Lung-carcinoma Patients and Matched Control Patients with Other Diseases, Subdivided by Place and Date of Interview*

Disease Group	Place and Date of Interview	Percentage Non-smokers	Percentage Smoking Daily*				No. Interviewed
			1 Cig.–	5 Cigs.–	15 Cigs.–	25 Cigs.+	
Carcinoma of lung (men)	Greater London, 1948–9	0·3	5·1	38·5	30·2	25·9	649
	Greater London, 1950–1	1·0	3·3	38·2	31·4	26·1	306
	Bristol, 1950–1	2·8	0·0	22·5	40·8	33·8	71
	Cambridge, 1951	0·0	0·0	50·0	29·4	20·6	34
	Leeds, 1950–1	0·0	1·9	47·2	34·0	17·0	53
	Newcastle, 1950–1	0·0	2·1	37·3	39·3	21·3	244
	Whole investigation	0·5	3·6	38·0	32·8	25·0	1,357
Control patients with other diseases (men)	Greater London, 1948–9	4·2	8·5	45·1	29·3	12·9	649
	Greater London, 1950–1	4·2	4·9	46·1	28·4	16·3	306
	Bristol, 1950–1	4·2	2·8	49·3	28·2	15·5	71
	Cambridge, 1951	2·9	8·8	52·9	29·4	5·9	34
	Leeds, 1950–1	5·7	7·5	39·6	35·8	11·3	53
	Newcastle, 1950–1	5·3	4·9	43·9	34·0	11·9	244
	Whole investigation	4·5	6·7	45·3	30·1	13·4	1,357
Carcinoma of lung (women)	Greater London, 1948–9	31·7	11·7	31·7	15·0	10·0	60
	Greater London, 1950–1	25·0	15·0	20·0	10·0	30·0	20
	Bristol, 1950–1	(50·0)†	—	(50·0)	—	—	2
	Cambridge, 1951	(50·0)	—	—	(50·0)	—	2
	Leeds, 1950–1	(20·0)	(20·0)	(60·0)	—	—	5
	Newcastle, 1950–1	68·4	15·8	15·8	—	—	19
	Whole investigation	37·0	13·0	27·8	11·1	11·1	108
Control patients with other diseases (women)	Greater London, 1948–9	53·3	20·0	16·7	10·0	0·0	60
	Greater London, 1950–1	55·0	10·0	20·0	10·0	5·0	20
	Bristol, 1950–1	(50·0)	(50·0)	—	—	—	2
	Cambridge, 1951	(50·0)	—	(50·0)	—	—	2
	Leeds, 1950–1	(60·0)	—	(40·0)	—	—	5
	Newcastle, 1950–1	57·9	15·8	26·3	—	—	19
	Whole investigation	54·6	16·7	20·4	7·4	0·9	108

* See footnote to Table III. † The percentages in parentheses are based upon very small numbers and have no reliability.

smokers among the lung-carcinoma patients than among the control patients. Amongst 1,357 men with carcinoma of the lung, only 7, or 0.5%, were non-smokers; there were 61, or 4.5%, among the same number of men with other diseases. At the other end of the scale, 25% of the men with lung carcinoma had smoked 25 or more cigarettes a day (or the equivalent in pipe tobacco); the proportion in the control patients was only 13.4%. Similarly, amongst the 108 women with carcinoma of the lung, 37.0% were non-smokers against 54.6% of the women with other diseases. Among women with carcinoma 11.1% had smoked 25 or more cigarettes a day; among those with other diseases this proportion was 0.9%.

These results are essentially the same as those recorded in our preliminary report. In Greater London, indeed, the results for the two periods 1948–9 and 1950–1 are remarkably alike (see Table IV, where they are set out separately and alongside figures from the provincial centres). Table IV also shows that the contrast between the smoking habits of the men in the two disease groups was observed quite consistently at the provincial centres. In each case the proportions of non-smokers and of men smoking less than five cigarettes a day were *lower*, and the proportion smoking 25 or more cigarettes a day was substantially *higher*, among the lung-carcinoma patients. In women similar results were obtained during the two periods of inquiry in Greater London, while at Bristol, Cambridge, and Leeds the numbers are too small to warrant attention. At Newcastle, however, the smoking habits of the female lung-carcinoma patients did not differ appreciably from those of their matched controls—in fact, the proportion of non-smokers was slightly higher in the lung-carcinoma group. Though the number interviewed was small (19 cases), the divergence from the experience of the lung-cancer groups elsewhere is sufficient to be statistically significant. Adding the provincial centres together gives the following figures for women:

	Non-smokers	Smoking 1–14 Cigs.	Smoking 15+ Cigs.	Total
Lung-carcinoma group ..	16	11	1	28
Control group	16	12	—	28

The presence of only one woman with lung carcinoma who had smoked 15 or more cigarettes a day is not, perhaps, surprising; it seems that very few women in the provinces smoke so much. Of all the 58 women interviewed at provincial centres, and who suffered from "other diseases" (other than lung carcinoma, carcinoma of other sites possibly related to tobacco, and carcinoma of uncertain primary site) none gave a history of smoking 15 or more cigarettes a day. In contrast, this amount was smoked by nearly 8% of 553 similar women with all other diseases interviewed in Greater London. There is, however, an absence in the provinces of any difference between the two groups in the numbers of non-smokers and of women smoking fewer than 15 cigarettes a day.

The "most recent amount smoked" will not necessarily give the best representation of a smoking history, even though defined, as here, to include the amount smoked by ex-smokers at the time they last gave up. Its advantage as a criterion is that the information is easily obtained and likely to be reasonably accurate. Its disadvantage is that smoking habits vary over a lifetime, sometimes considerably, and previous habits, which may be relevant, are being ignored. We have therefore calculated other quantitative estimates of the amount smoked as revealed in the patient's history. These are (*a*) the amount smoked immediately before the patient's illness, (*b*) the maximum amount ever smoked regularly, (*c*) the total amount smoked since smoking was begun, and (*d*) the average amount smoked daily over the 10 years preceding the patient's illness, over the penultimate 10 years, and over the whole of the patient's life since the age of 15, taking into account recorded changes during these periods.

Qualitatively similar results are obtained whichever of these estimates is used. The sharpest differentiation between the lung-carcinoma and control patients, for both men and women, appears to be given by the average daily amount smoked over the 10 years preceding the patient's illness. The results of this calculation are shown in Table V and differences between the groups of patients—particularly in the women—are more pronounced than those in Table III.

For men, the amount smoked immediately before the patient's illness is equally good, but the estimates of the total amount consumed throughout life, the average daily amount since the age of 15, and the average daily amount over the penultimate 10 years give differences only of the same order as those shown by "the most recent amount smoked"; the maximum daily amount ever smoked differentiates the groups less clearly. For women, all the estimates except the amount smoked immediately before the patient's illness are more discriminating than "the most recent amount smoked," though the maximum daily amount ever smoked gives only a slightly increased divergence between the two groups.

In view of these results with varying measures of the smoking history we have used in subsequent tables *the average amount smoked daily over the 10 years preceding the patient's illness* as the most appropriate criterion. A whole life history should perhaps be a truer measure of the "exposure to risk," but, as we pointed out in our previous paper, too much inaccuracy may result from requiring the patient to remember habits of many years past.

The Duration of Smoking

Comparisons of the ages at which the patients reported that they began to smoke, the number of years they had smoked, and, when appropriate, the number of years since they last gave up are shown in Table VI.

The lung-carcinoma patients are seen, on the average, to have begun smoking rather earlier, to have continued longer, and to have been rather less inclined to stop. In men, these differences are all statistically significant. In women they are not significant, but they are in the same direction, and no less distinct, so that it is reasonable to accept them as real.

The most pronounced difference appears in the number of years since smoking had last been given up. Since the control group contained more light smokers (Table III) the higher proportion of ex-smokers in it here seen might, it was thought, be due to the fact that it is light smokers who more readily give up. In fact, the opposite appeared to be true. Of the 124 male control patients who had given up smoking nearly one-third (31.5%) were smoking 25 or more cigarettes a day when they gave up; of those who continued to smoke, only 12.2% consumed as much.

TABLE V.—*Average Amount of Tobacco Smoked Daily Over the 10 Years Preceding the Onset of the Present Illness; Lung-carcinoma Patients and Matched Control Patients with Other Diseases*

Disease Group	No. of Non-smokers	No. Smoking Daily Average* of				
		Less than 5 Cigs.	5 Cigs.–	15 Cigs.–	25 Cigs.–	50 Cigs.+
Men:						
1,357 lung-carcinoma patients (99·9%) ..	7 (0·5%)	55 (4·0%)	489 (36·0%)	475 (35·0%)	293 (21·6%)	38 (2·8%)
1,357 control patients with other diseases (100%)	61 (4·5%)	129 (9·5%)	570 (42·0%)	431 (31·8%)	154 (11·3%)	12 (0·9%)
Women:						
108 lung-carcinoma patients (100%)	40 (37·0%)	16 (14·8%)	24 (22·2%)	14 (13·0%)	14 (13·0%)	0
108 control patients with other diseases (100%) ..	59 (54·6%)	25 (23·1%)	18 (16·7%)	6 (5·6%)	0 (0·0%)	0

Difference between proportions of smokers smoking different amounts—Men: $\chi^2=93·77$, n=4, $P<0·000001$. Women: $\chi^2=17·41$, n=3, $P<0·001$.
* Ounces of tobacco have been expressed as being equivalent to so many cigarettes. There is 1 oz. of tobacco in 26·5 normal-size cigarettes, so that the conversion factor has been taken as: 1 oz. of tobacco a week = 4 cigarettes a day.

TABLE VI.—*Age at Starting to Smoke, Number of Years Smoked, and Number of Years Since Smoking was Given Up, Lung-carcinoma Patients and Matched Control Patients*

Sex	Age at Starting	Lung-carcinoma Patients		Control Patients		No. of Years Smoking	Lung-carcinoma Patients		Control Patients		No. of Years Given Up	Lung-carcinoma Patients		Control Patients	
		No.	%	No.	%		No.	%	No.	%		No.	%	No.	%
Men	Under 20	1,077	79·8	992	76·5	1–	12	3·4	15	6·2	0–	1,280	94·8	1,172	90·4
	20–	251	18·6	264	20·4	10–	34		65		1–	56	4·1	75	5·8
	30–	18	1·6	33	3·1	20–	746	55·3	725	55·9	10–	6	1·0	26	3·8
	40+	4		7		40+	558	41·3	491	37·9	20+	8		23	
	All ages	1,350	100·0	1,296	100·0	All periods	1,350	100·0	1,296	100·0	All periods	1,350	99·9	1,296	100·0
	$\chi^2=7·95$; n=2; 0·01<P<0·02					$\chi^2=12·66$; n=2; P<0·01					$\chi^2=25·87$; n=2; P<0·001				
Women	Under 20	20	29·4	12	24·5	1–	14	38·2	18	53·1	0–	58	85·3	41	83·7
	20–	23	33·8	15	30·6	10–	12		8		1–	9	13·2	6	12·2
	30–	10	36·8	7	44·9	20–	36	52·9	20	40·8	10–	0	1·5	0	4·1
	40+	15		15		40+	6	8·8	3	6·1	20+	1		2	
	All ages	68	100·0	49	100·0	All periods	68	99·9	49	100·0	All periods	68	100·0	49	100·0

The Method of Smoking

So far the only distinction we have drawn between smokers is in the *quantity* of tobacco consumed. There are, however, qualitative differences which might be important—namely, whether the smoker inhales, smokes a pipe, uses a cigarette holder, smokes filter-tipped cigarettes, rolls his own cigarettes, or lights his tobacco with matches or a petrol lighter.

Inhaling.—All the smokers and ex-smokers were asked whether they inhaled (with the exception of three lung-carcinoma and two control patients, in whom the question was inadvertently omitted). Of 1,415 lung-carcinoma patients (men and women), 64.6% said yes and 35.4% said no; of the 1,343 control patients with other diseases, 66.6% said yes and 33.4% said no. The differences are negligible. Similar results were obtained for men and women considered separately. (Further consideration is paid to inhaling in the section dealing with site of tumour.)

Cigarettes and Pipes.—Some persons usually smoke cigarettes, others usually smoke a pipe. Habits, however, do not remain constant, and it has been necessary to divide male smokers into three broad categories: (*a*) those who have never smoked a pipe regularly for as long as one year (" pure cigarette-smokers "); (*b*) those who have smoked cigarettes and a pipe; and (*c*) those who have never smoked cigarettes regularly for as long as one year (" pure pipe-smokers "). Among the 1,350 male lung-carcinoma patients who smoked, 3.9% were pure pipe-smokers and 74.4% were pure cigarette-smokers; among the 1,296 male control patients who smoked the corresponding proportions were 6.9% and 69.4%. The differences, though not striking, are statistically highly significant (χ^2 for the three groups, pure pipe, mixed, pure cigarette=15.85; n=2, P<0.001). It would appear that pipe-smoking is less closely associated with the development of lung carcinoma than cigarette-smoking. Pipe-smokers, however, consume, on the average, less tobacco than cigarette-smokers, and this must account for some of the relative deficiency of pipe-smokers in the lung-carcinoma group. It does not seem that it can account for the whole difference, since the proportion of pure pipe-smokers is somewhat lower at each level of tobacco consumption. The relevant figures are as follows:

	Percentage of Pure Pipe-smokers among all Smokers at Each Average Daily Consumption Level (Measured in Terms of Cigarettes)			
	Less than 5 Cigs.	5 Cigs.–	15 Cigs.–	25 Cigs.+
Male lung-carcinoma patients	9·1%	7·2%	1·3%	2·1%
Male control patients with other diseases	10·9%	10·5%	3·5%	2·4%

On the other hand, studying the pure pipe-smokers alone we find that 9.4% of those with lung-carcinoma smoked the equivalent of less than five cigarettes a day and 13.2% smoked the equivalent of 25 or more a day; in the control group the proportions were 15.1% and 4.3%. In other words, a higher proportion of the pure pipe-smokers with carcinoma of the lung fall into the higher smoking categories —as with the cigarette-smokers.

We conclude, as in our earlier report, that the method of smoking is of importance and that smoking a pipe, though also related to carcinoma of the lung, appears to carry a smaller risk than smoking cigarettes (see also section on estimated risks).

Cigarette-holders.—A possible explanation of this lower risk of pipe-smoking is that the pipe-stem acts as a partial filter of a carcinogenic agent. If that were so, we might expect that fewer of the patients with carcinoma of the lung had used cigarette-holders. We sought information on this point in the latter stages of the inquiry—from the last 523 pairs of male lung-carcinoma and control patients to be interviewed. Judged by the proportions of non-smokers and pure pipe-smokers in the two groups, these last patients seem to be a representative sample of the total. Table VII shows results obtained from them. Few

TABLE VII.—*Use of Cigarette-holders: Male Lung-carcinoma and Matched Control Patients. (Information Obtained During the Last Part of the Investigation Only)*

Disease Group	Non-smokers	Never Smoked Cigarettes	Cigarette-smokers. Holders Used			Total Cigarette-smokers
			Never	Occasionally	Regularly	
523 lung-carcinoma patients	4	15	479	15	10	504
523 control patients	26	30	413	27	27	467

patients had ever used holders, but the proportion of cigarette-smokers who had done so was significantly smaller in the group with carcinoma of the lung (5%) than in the control patients (12%) ($\chi^2=14.74$, n=2, P<0.001).

This difference might merely be due to an association between using a holder and light smoking, but the available evidence suggests not. Among the 54 cigarette-smokers in the control group who had used holders five (9%) smoked an average of fewer than 15 cigarettes a day and six (11%) smoked an average of 25 or more; the corresponding figures for the 413 cigarette-smokers who had not used holders were 32 (8%) and 55 (13%). Further evidence that an association with light smoking cannot account for the relative deficiency of users of cigarette-

holders in the lung-carcinoma group is the finding that the proportion who had used holders was lower at each level of tobacco consumption—namely:

	Percentage of Cigarette-smokers who had ever used Holders at Each Average Daily Consumption Level			
	Less than 5 Cigs.	5 Cigs.–	15 Cigs.–	25 Cigs.+
Male lung-carcinoma patients who smoked cigarettes	5·9%	4·0%	6·0%	4·5%
Male control patients with other diseases who smoked cigarettes	13·5%	12·6%	10·4%	9·8%

Types of Cigarettes.—Cigarette-smokers were asked whether they bought manufactured cigarettes or bought tobacco and rolled their own. Of the 1,297 male lung-carcinoma patients who had ever smoked cigarettes 20.7% smoked mostly hand-rolled cigarettes; of the 1,203 similar control patients the proportion was 19.1%. Evidently there is no specific association of manufactured, as opposed to hand-rolled, cigarettes and carcinoma of the lung. It can also be concluded that the different risks associated with cigarette- and pipe-smoking are unlikely to be the result of the different types of tobacco consumed, as a number of men who roll their cigarettes use pipe tobacco.

In view of the presence of arsenic in American tobacco and its almost complete absence from Oriental tobacco (Daff and Kennaway, 1950) it was clearly of interest to determine whether there was any difference in the proportions of American and "Turkish" tobacco smokers in the lung-carcinoma and control groups. The results of such inquiry were inconclusive because nearly all smokers had habitually smoked "Virginian." In fact, only one smoker was found who had never regularly smoked it (a man of 70, under treatment for an enlarged prostate). Of the 504 male lung-carcinoma patients who had smoked cigarettes only 3.8% said that they had, at some period, regularly smoked Turkish tobacco; among the 467 control patients the figure was 4.5%. The difference is statistically insignificant.

During the last part of the investigation inquiries were also made about the brands of cigarettes smoked and the use of filter-tipped cigarettes. The results (Table VIII) show that none of the four main brands recorded was more closely associated with carcinoma of the lung than another. The proportions are remarkably similar in the two groups of patients. On the other hand, very few of the men with lung carcinoma had ever regularly used filter-tipped cigarettes

TABLE VIII.—*Brands of Cigarettes Smoked and Use of Filter-tipped Cigarettes: Male Lung-carcinoma and Matched Control Patients. (Information Obtained During the Last Part of the Investigation Only)*

Type of Smoker	Lung-carcinoma Patients	Control Patients
Cigarette-smokers, smoking manufactured cigarettes—		
Brand mainly smoked:		
Brand A	72 (18·2%)	70 (19·4%)
„ B	11 (2·8%)	14 (3·9%)
„ C	123 (31·1%)	107 (29·6%)
„ D	21 (5·3%)	15 (4·2%)
Other brands	36 (9·0%)	39 (10·8%)
Mixed „	133 (33·6%)	116 (32·1%)
All brands	396 (100·0%)	361 (100·0%)
Brand not stated (present smokers of hand-rolled cigarettes or pipes)	108	106
All cigarette-smokers	504	467
Cigarette-smokers, filter-tipped cigarettes:		
Ever smoked regularly*	3	15
Never „ „	501	452
All cigarette-smokers	504	467

* For one or more years.

—3 in 504 compared with 15 in the 467 controls. The difference is significant ($\chi^2=7.74$, $n=1$, $P<0.01$), but with so few observations the conclusions to be drawn must be highly speculative. The explanation may be that filter-tipped cigarettes are smoked predominantly by light smokers, but we have insufficient data to test that possibility.

Use of Petrol Lighters.—In the two groups of 523 male patients last interviewed inquiry was made into the use of petrol lighters. Of the 504 male patients with carcinoma of the lung who smoked cigarettes, 42.9% reported that at some period they had regularly used petrol lighters; of the 468 similar control patients, the proportion was 41.3%. The difference is negligible, and the evidence is against the hypothesis—often put forward—that petrol lighters are the responsible carcinogenic agent.

Use of Tobacco for Chewing and as Snuff.—Although extraneous substances will be brought into contact with the bronchial mucosa more readily by smoking than by chewing or by snuff, it is possible that particles of tobacco are inspired into the bronchial tree by these latter means and that these uncombusted particles are carcinogenic. The possibility is suggested by the frequent occurrence of cancer of the buccal cavity in Eastern countries where the inhabitants have the habit of chewing quids of tobacco mixed with flavouring agents.

Questions about chewing tobacco and the use of snuff were asked of 1,209 male patients with lung carcinoma and of the 1,209 corresponding control patients.* The results show (Table IX) that fewer patients with lung carcinoma

TABLE IX.—*Use of Tobacco for Chewing and as Snuff: Male Lung-carcinoma and Matched Control Patients. (Information Obtained During Part of the Investigation Only)*

Disease Group	Tobacco Never Chewed	Tobacco Chewed				Total who had Chewed Tobacco
		Occasionally		Regularly		
		Less than 10 Yrs.	10 Yrs.+	Less than 10 Yrs.	10 Yrs.+	
1,209 lung-carcinoma patients	1,169	8	4	11	17	40
1,209 control patients	1,145	6	9	17	32	64
	Tobacco Never Taken as Snuff	Tobacco Taken as Snuff				Total who had Taken Tobacco as Snuff
1,209 lung-carcinoma patients	1,176	8	7	10	8	33
1,209 control patients	1,166	11	5	16	11	43

Significance tests of differences between lung-carcinoma and control patients:
Chewing: $\chi^2=5·79$, $n=1$, $0·01<P<0·02$.
Snuff-taking: $\chi^2=1·36$, $n=1$, $0·20<P<0·30$.

had chewed tobacco (40, or 3.3%, against 64, or 5.3%) and slightly fewer had ever taken snuff (33, or 2.7%, against 43, or 3.6%); the differences are small though statistically significant for chewing. That this latter difference is likely to be real is borne out by the fact that it is more marked for those who had chewed regularly (28 to 49) than for those who had done so occasionally (12 to 15), and most marked for those who had chewed regularly for more than 10 years (17 to 32). The number of patients who were still in the habit of chewing was too small for it to be possible to assess the amount they smoked in comparison with others. It may be that there were fewer lung-carcinoma patients who had chewed tobacco because men who chew will smoke less.

*After the completion of the first part of the investigation these questions were temporarily omitted from the questionary, and 148 male patients with lung carcinoma interviewed outside London and their corresponding control patients were not asked whether they chewed tobacco or used snuff.

Nature of the Carcinoma in Relation to Smoking

Histological Type

According to Wynder and Graham (1950), adenocarcinoma of the lung is less closely related to smoking than the other histological types of lung carcinoma. Primary adenocarcinoma of the lung is an uncommon condition, but of particular interest, in relation to smoking, in that it has invariably been reported as being relatively commoner in women than in men. In the present series, all patients with a histologically confirmed diagnosis (approximately 70% in each sex) have been divided according to type, with the following results:

	Histological Type				
	Epidermoid	Oat-cell or Anaplastic	Adeno-carcinoma	Unclassified	No Histological Confirmation
1,357 men ..	475 (52%)	303 (33%)	33 (4%)	105 (11%)	441
108 women	18 (23%)	38 (48%)	10 (13%)	13 (16%)	29

In Table X the numbers of men and women smoking different amounts of tobacco are shown separately for each histological type of growth and are compared with the numbers expected from the experience of all male and all female patients in whom the diagnosis was confirmed histologically. There is no statistically significant difference between the amounts smoked by patients in the different histological groups in either sex. The number of proved cases of adenocarcinoma is, however, too small (43) to conclude that no difference exists. There were, in fact, relatively more non-smokers and very light smokers (average consumption less than five cigarettes a day) among the patients with adenocarcinoma in both sexes, and it is possible that larger numbers would have supported Wynder and Graham's findings.

Table X also shows that it is not possible to detect any difference, in amount smoked, between the cases diagnosed clinically and those in whom the diagnoses were histologically confirmed. This result suggests that the "clinical" diagnoses were generally accurate—which is not surprising, since they were based on findings at thoracotomy or at necropsy in 93 (19.8%), on direct observation of the tumour bronchoscopically in a further 96 (20.4%), while in many of the remainder bronchoscopic examination suggested the presence of a carcinoma though no tumour was seen.

Site of Tumour

The site of origin of a tumour within the lung may be of interest, since it is possible that aetiological agents might reach the main bronchi but not the bronchioles and alveoli. In the present series 1,154 (90.4%) were considered to have arisen centrally and 122 (9.6%) peripherally (in 189 it was not possible to decide).

Analysis of the smoking habits of the patients in these two groups reveals no difference between them in the amounts smoked but a slight difference in the prevalence of inhaling. (See Table XI. The comparison here does not allow for differences in age distribution of the patients with central and peripheral growths, but these differences are small and do not materially affect the results.) It will be seen that a slightly higher proportion of the males with peripheral growths inhaled regularly (62.6%) compared with

TABLE X.—*Average Amount of Tobacco Smoked Daily Over the 10 Years Preceding the Onset of the Present Illness, Divided According to Histological Type: Lung-carcinoma Patients*

Histological Type	No. of Non-smokers	Average Amount Smoked Daily over 10 Years. Number Smoking:			
		Less than 5 Cigs.	5 Cigs.–	15 Cigs.–	25 Cigs.+
			Men		
A					
Epidermoid carcinoma (475)	1 (2·4)*	14 (19·3)	169 (166·9)	175 (172·4)	116 (114·1)
Oat-cell or anaplastic carcinoma (303)	2 (1·8)	12 (11·2)	110 (106·7)	105 (111·4)	74 (72·0)
Adenocarcinoma (33)	2 (0·2)	2 (0·9)	7 (11·5)	16 (12·3)	6 (8·2)
Type unclassified (105)	0 (0·6)	8 (4·7)	36 (37·0)	38 (38·0)	23 (24·8)
B					
Histological evidence obtained (916) ..	5 (4·9)	36 (34·5)	322 (328·5)	334 (322·4)	219 (225·8)
No histological evidence (441)	2 (2·1)	19 (20·5)	167 (160·5)	141 (152·6)	112 (105·2)
			Women		
C					
Epidermoid carcinoma (18)	11 (8·6)	1 (1·9)	4 (4·3)	1 (1·6)	1 (1·6)
Oat-cell or anaplastic carcinoma (38) ..	12 (11·2)	6 (5·1)	9 (10·0)	7 (7·4)	4 (4·3)
Adenocarcinoma (10)	5 (3·8)	2 (1·2)	1 (2·7)	0 (1·4)	2 (1·0)
Type unclassified (13)	1 (5·5)	2 (1·8)	5 (3·0)	4 (1·6)	1 (1·1)
D					
Histological evidence obtained (79) ..	29 (28·7)	10 (11·1)	20 (18·4)	12 (10·9)	8 (10·1)
No histological evidence (29)	11 (11·3)	5 (3·9)	5 (6·6)	2 (3·2)	6 (4·0)

* The figures in parentheses are the numbers that would have occurred if the patients in the histological group in question had had, at each age, exactly the same smoking habits as all the patients with which the group is being compared. That is, in part A of the table, all male patients with histological evidence of the growth; in part B, all male patients; in part C, all female patients with histological evidence of the growth; in part D, all female patients.

TABLE XI.—*Prevalence of Inhaling: Patients with Carcinoma of the Lung Arising Centrally and Peripherally and Corresponding Matched Control Patients*

Disease Group	No. of Smokers Inhaling			Total No. of Smokers	No. of Non-smokers
	Regularly	Occasionally	Never		
Male lung-carcinoma patients with:					
1,070 central growths	558 (52·4%)	126 (11·8%)	380 (35·7%)	1,064 (99·9%)	6
116 peripheral growths	72 (62·6%)	13 (11·3%)	30 (26·1%)	115 (100%)	1
Male control patients corresponding to lung-carcinoma patients with:					
1,070 central growths	583 (57·1%)	116 (11·4%)	322 (31·5%)	1,021 (100%)	49
116 peripheral growths	63 (53·3%)	12 (10·5%)	39 (34·2%)	114 (100%)	2
Female lung-carcinoma patients with:					
84 central growths	24	6	17	47	37
6 peripheral growths	1	1	3	5	1
Female control patients corresponding to lung-carcinoma patients with:					
84 central growths	14	5	20	39	45
6 peripheral growths	0	0	1	1	5

Significance tests. Prevalence of inhaling (regular plus occasional):
Male lung-carcinoma patients, central compared with peripheral growths: $\chi^2=4{\cdot}24$, $n=1$, $0{\cdot}02<P<0{\cdot}05$.
Male patients, patients with central growths compared with corresponding controls: $\chi^2=4{\cdot}07$, $n=1$, $0{\cdot}02<P<0{\cdot}05$
Male patients, patients with peripheral growths compared with corresponding controls: $\chi^2=1{\cdot}79$, $n=1$, $0{\cdot}10<P<0{\cdot}20$.

the men with central growths (52.4%)—a statistically significant difference (0.05 level). The patients in each group can also be compared with their own matched controls. It is then found that the males with central growths include rather fewer regular inhalers than their controls (52.4 to 57.1%), while the group with peripheral growths contain rather more (62.6 to 53.3%). The difference is statistically significant in the former case but not in the latter, where the observations are too few to eliminate chance as an explanation. With the women the numbers are too small to warrant consideration.

Estimated Risks

Amount of Smoking

To measure approximately the relative risks associated with different levels of smoking we need to know (*a*) the number of people smoking different amounts of tobacco in each age group—that is, the numbers "at risk"—and (*b*) the number of people smoking different amounts in each age group who died from carcinoma of the lung. It would then be possible, because of the very high fatality of the disease, to equate the calculated death rates to the risks of developing it.

The present investigation cannot provide estimates of these figures for the whole country, since the patients interviewed were drawn mainly from Greater London, and smoking habits and the lung-cancer death rate both vary between countryside and town. For example, in 1949 the report of the Registrar-General shows that the recorded death rates from lung cancer in men were 597, 521, 398, and 292 per million in, respectively, Greater London, county boroughs outside Greater London, other urban districts, and rural districts.

For the Greater London area alone we may, however, proceed on three assumptions—namely, (*a*) that the smoking habits reported by the control patients without carcinoma of the lung who lived in Greater London at the time of their interview are, at each age and in each sex, typical of the inhabitants of Greater London generally; (*b*) that the smoking habits reported by the patients with carcinoma of the lung, also living in Greater London at the time of their interview, are typical of the inhabitants who died of the disease during the period of the survey; and (*c*) that the deaths attributed by the Registrar-General to lung cancer both in men and in women provide a reasonable estimate of the actual numbers of deaths due to carcinoma of the lung. On these assumptions, which are bold but, we think, not wholly unreasonable, we can calculate, for the one region, death rates for each level of tobacco consumption.

The population of Greater London given by the Registrar-General for June 30, 1950, has been taken as the population at risk. The numbers of persons within this population smoking different amounts of tobacco have been estimated from the data for each sex and for each of the age groups 25–44, 45–64, and 65–74.

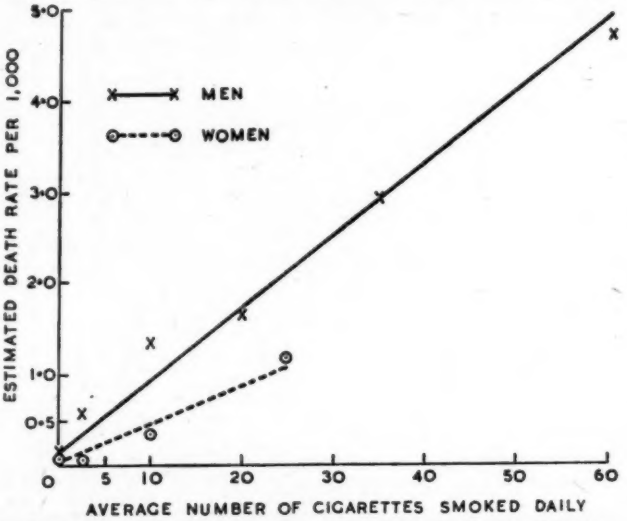
Thus at ages 45–64 we had 932 male patients resident in Greater London with diseases other than lung carcinoma; 4.1% were non-smokers, 9.3% had smoked an average over the preceding 10 years of fewer than five cigarettes (or their equivalent) a day, 42.6% an average of 5–14 a day, 29.9% an average of 15–24 a day, 12.8% an average of 25–49 a day, and 1.3% an average of 50 or more a day. The male population of Greater London at ages 45–64 was 937,000, and this population has been given the above proportions of non-smokers and smokers of different amounts. (In making these estimates we ignore the lung-carcinoma patients in the total population, but their proportion is too small to make any material difference.) In the same way the numbers of persons of each sex and age dying from lung cancers in Greater London in 1950 have been divided up on the basis of the smoking habits of the lung-carcinoma patients who were interviewed.

The death rates thus obtained (Table XII) increase with both age and amount smoked. They pass from a negligible figure for male non-smokers aged 25–44 to a level of the order of 1 in 100 per year among men aged 65–74 who have smoked an average of 25 cigarettes or more a day for the preceding 10 years. The greatest number of our subjects were aged 45–64, and the rates for this group should therefore be the most reliable. In the Chart these are shown graphically against the amounts smoked. It appears, on the assumptions made, that the death rate increases in approximately simple proportion with the amount smoked. Among women the death rate seems to rise more slowly, but the numbers are smaller and considerably less reliable.

TABLE XII.—*Estimated Annual Death Rates from Lung Cancer per 1,000 Men and per 1,000 Women Living in Greater London; by Age Group and Average Amount of Tobacco Smoked Daily in Preceding 10 Years**

Sex and Age	Annual Death Rate per 1,000 Persons						No. of Lung-carcinoma Patients Interviewed
	Non-smokers	Average Amount Smoked Daily in Preceding Ten Years					
		Less than 5 Cigs.	5 Cigs.–	15 Cigs.–	25 Cigs.–	50 Cigs.+	
Men							
25– ..	*0·00*†	*0·03*	0·13	0·12	0·17	*0·52*	61
45– ..	*0·14*	0·59	1·35	1·67	2·95	4·74	539
65–74 ..	*0·00*	2·38	2·66	3·88	6·95	*10·24*	130
Women							
25– ..	*0·006*	*0·04*	*0·03*	*0·13*		—	9
65– ..	0·09	*0·06*	0·34	1·19		—	39
45–74 ..	0·32	*0·70*	*0·59*	*2·37*		—	13

* The reasons for the adoption of this measure of smoking habits is explained in the text (see section on amount smoked).
† Rates based on observation of fewer than five cases of carcinoma of the lung are given in italics.



Estimated annual death rates from lung cancer in Greater London for men and for women aged 45–64, in relation to the average amount of tobacco smoked daily (measured in terms of cigarettes) in the preceding 10 years.

Cigarettes or Pipe

On the same assumptions, that our data are representative of Greater London, it is also possible to estimate mortality rates for each type of smoker—that is, cigarettes only, cigarettes and pipe, pipe only. As previously shown, the pure pipe-smokers are few and we can therefore calculate rates only for the one broad age group 45–74. The results are:

	Estimated Annual Mortality Rates from Lung Cancer per 1,000 Men Aged 45–74. Average Amount Smoked Daily for Preceding 10 Years in Terms of Cigarettes*				
	Less than 5 Cigs.	5 Cigs.–	15 Cigs.–	25 Cigs.–	50 Cigs.+
Pure cigarette-smokers ..	1·11	1·71	2·16	3·50	7·37
Smokers of cigarettes and pipe	0·87	1·67	1·98	3·35	*2·24*†
Pure pipe-smokers	*0·95*†	1·35	*0·79*†	*2·08*†	—
All smokers ..	1·04	1·66	2·05	3·42	5·42

* See footnote to Table III. † Based on fewer than 5 cases.

At each smoking level the estimated death rate of pipe-smokers is less than that of cigarette-smokers, and the difference increases with heavier smoking. In three of the four groups the death rate of those smoking cigarettes and pipe is intermediate. With the amount of data at our disposal and the assumptions made in calculating these rates we would be reluctant to draw any precise conclusion on the relative level of the risks. But it certainly appears that the risks are less in pipe-smokers than in cigarette-smokers, and perhaps to the greatest extent in the heavier-smoking categories.

Town and Country

There seem to be differences in smoking habits between townsmen and countrymen (briefly referred to above), and our data may be used to see whether they can wholly, or partially, account for the reported different mortality rates from carcinoma of the lung—though they are insufficient to give more than an approximate answer. The patients interviewed in this inquiry lived in different parts of the country. Grouping them according to place of residence, we can roughly estimate the smoking habits of persons living in Greater London, county boroughs, urban districts, and rural districts. There were, however, relatively few patients living in the country, and a special survey was therefore made (in February, 1950) of the smoking habits of 531 other patients, aged 25–74, admitted to hospitals in rural areas of Dorset and Wiltshire.

TABLE XIII.—*Smoking Habits of Male Patients Living in Different Parts of the Country; Divided According to Density of Population. (Standardized to age distribution of population of England and Wales, aged 25–74)*

Area of Residence	Percentage of Non-smokers	Percentage Smoking Daily Average of				Percentage of			No. of Patients Interviewed
		Less than 5 Cigs.	5 Cigs.–	15 Cigs.–	25 Cigs.+	Pure Cigarette-smokers	Cigarette and Pipe-smokers	Pure Pipe-smokers	
Greater London ..	5·1	8·3	38·3	33·7	14·6	74·2	16·0	4·8	1,393
County borough ..	6·8	6·6	42·7	34·0	9·9	66·3	22·8	4·1	240
Other urban district ..	8·4	13·3	37·1	32·3	8·9	59·9	23·9	7·8	439
Rural district	10·4	13·7	40·8	27·6	7·7	58·4	21·5	9·8	327

To facilitate comparisons the male inhabitants of England and Wales between the ages of 25 and 74 have been taken as a standard population, and the smoking habits in this population have been estimated from the incidence rates of smoking actually observed in the age groups in each of the four areas (Table XIII). It appears that as the place of residence becomes more highly urbanized the proportion of non-smokers and of pure pipe-smokers decreases and the proportion of heavier smokers and pure cigarette-smokers increases. Thus the changes are in the direction which would lead to a higher death rate from carcinoma of the lung in the towns. Whether they can account for the observed differences in mortality is difficult to say. On the assumption that the estimated death rates of Table XII should prevail equally in all areas, it would seem that the recorded differences in mortality between town and country are greater than could be attributed wholly to the differences in smoking habits. In other words, the differences in smoking habits shown in Table XIII are not sufficient to lead to a rural mortality rate which is only about half that of the large towns.

Other Aetiological Factors

The inquiry here reported was designed to throw light on any aetiological agent in carcinoma of the lung—for example, on substances which pollute the atmosphere. The questions on smoking were merely one facet of the investigation. We now turn to other aspects.

Occupation and Social Class

Occupational histories were taken from all patients, but these reveal no gross association between any type of occupation and lung carcinoma which might indicate an aetiological agent of general significance—for example, persons occupationally exposed to motor fumes or road dust do not appear more frequently in the lung-carcinoma group. The results will be published in full later.

Social class has already been considered (Table II); it showed no significant difference between the male patients with lung carcinoma and their controls. This observation is in keeping with the Registrar-General's 1930–2 decennial supplement on occupational mortality, though in the present inquiry the lack of association may be overemphasized from the fact that our control patients were usually, and deliberately, taken from the same hospitals as the patients with carcinoma of the lung. This designed equality in some respects may give an overestimated equality in social class.

Place of Residence

The Registrar-General's evidence that cancer of the lung is more frequent in the large towns than in the smaller towns and countryside suggests that a higher proportion of our lung-carcinoma patients would be expected to have been living in Greater London and the county boroughs. In fact, as shown in Table II, this was not the case. If, however, the patients' places of residence are analysed separately, for those interviewed in Greater London and those interviewed in the provinces, a different picture is obtained (Table XIV).

Of patients interviewed in Greater London, fewer with lung carcinoma lived there (76%) compared with the controls (87%); more lived in each of the other types of area. Of patients interviewed in the provinces, more with lung carcinoma lived in the county boroughs (45% against 38%) and fewer lived in rural districts (22% against 28%).

The differences in Greater London can reasonably be explained on the grounds that patients with cancer living outside London tend, more than patients with other diseases, to come to London for treatment. In the provinces, however, the control patients with other diseases were interviewed in hospitals which were deliberately chosen because, like the thoracic units, they also served as regional centres. Consequently there should not be on demographic grounds any deficiency among them of patients living in the smaller towns or in the countryside. It would be reasonable to suspect that any difference between the places of residence

TABLE XIV.—*Place of Residence: Lung-carcinoma and Matched Control Patients, Subdivided by Place of Interview*

Place of Residence	Place of Interview			
	Greater London		Provinces	
	Lung-carcinoma Patients	Control Patients	Lung-carcinoma Patients	Control Patients
Greater London	791	900	0	0
Other county boroughs ..	31	16	194	165
Other urban districts ..	133	71	142	142
Rural districts	62	42	93	122
Abroad	18	6	1	1
All places	1,035	1,035	430	430

Difference between places of residence:
Patients interviewed in Greater London: $\chi^2=40{\cdot}50$, $n=4$, $P<0{\cdot}001$.
Patients interviewed in provinces (excluding patients residing abroad): $\chi^2=6{\cdot}25$, $n=2$, $0{\cdot}02<P<0{\cdot}05$.

of patients in the lung-carcinoma and control groups would reflect differences in the relative incidence of the conditions in the different areas. The observation in the provinces that a smaller proportion of the lung-carcinoma than of the control patients lived in the country supports, therefore, the contention that lung carcinoma is less common in rural than in urban areas.

Evidence can also be obtained by comparing, for patients living in a given type of area at the time of interview, the proportion who had previously lived for any long time in the countryside (see Table XV). Among the lung-carcinoma patients living in Greater London at the time of interview, 4.3% had previously lived for 10 or more years in a rural district; among control patients living in Greater London

TABLE XV.—*Residence for 10 or More Years in the Countryside: Lung-carcinoma and Matched Control Patients, Subdivided by Place of Residence at the Time of Interview*

Residence at Time of Interview	Lung-carcinoma Patients			Control Patients		
	No. Interviewed	Lived for 10 or More Years in a Rural District		No. Interviewed	Lived for 10 or More Years in a Rural District	
		No.	%		No.	%
Greater London ..	791	34	4·3	900	62	6·9
Other county boroughs ..	225	13	5·8	181	12	6·6
Other urban districts ..	275	37	13·5	213	32	15·0
Rural districts ..	155	136	87·7	164	149	90·9
Abroad	19	1	—	7	0	—
All places ..	1,465	221	(15·1)	1,465	255	(17·4)

the proportion was 6.9%. For each type of area this proportion is lower among the lung-carcinoma patients. The differences, though slight, are consistent and in conformity with the previous conclusion. They are not, however, statistically significant ($\chi^2=6.45$, n=4, $0.10<P<0.20$).

Residence Near a Gasworks

Gasworkers have been reported as specially liable to carcinoma of the lung (Kennaway and Kennaway, 1947; Doll, 1952), and it was therefore thought possible that residence near a gasworks with inhalation of its fumes might conduce to the disease. All the patients were asked whether they had ever lived near a gasworks and, if so, for how long. The results revealed no difference: 23.0% (337/1,465) of the lung-carcinoma patients and 21.5% (315/1,465) of the control patients had lived near a gasworks for a year or more ($\chi^2=0.95$, n=1, $0.30<P<0.50$). This result agrees with that obtained by McConnell, Gordon, and Jones (1952).

Exposure to Different Forms of Heating

Further information on the possible effects of exposure to coal-gas was sought by asking the form of heating used in the houses in which the patients had lived. This question also related to the possibility that exposure to benzpyrene in the soot of domestic fires might be conducive to the development of carcinoma. Analysis was made of the kinds of heating used in the living-rooms of all the houses in which the patients had resided for three or more years, and the numbers of years were calculated that each patient had been exposed, in his living-room, to a coal fire, a gas fire, an electric fire, an anthracite stove, a radiator, or other form of heating. The results (Table XVI) reveal very little difference in the histories given by the two groups of patients.

Previous Respiratory Illnesses

A large number of the control patients had some respiratory disease, and we clearly cannot assume that the history of previous respiratory illnesses given by these patients would be characteristic of other patients generally. It would not, therefore, be proper to compare the lung-carcinoma patients with the general control groups of patients to determine whether previous respiratory illnesses play any part in the aetiology ot carcinoma of the lung. We have accordingly compared lung-carcinoma patients with patients with other forms of cancer (mainly stomach and large bowel, and excluding those in whom the site of origin of the growth was in no doubt and also those with growths elsewhere in the chest, upper respiratory passages, and mouth).

The general cancer group was not selected to be of the same sex and age distribution as the lung-carcinoma group, and it is therefore necessary to allow for sex and age differences between them. For this purpose we have first calculated for *all* the cancer patients put together—lung, stomach, large bowel, etc.—the reported incidence of previous respiratory illness in each sex and 10-year age subgroup. These rates we have then applied to the numbers of patients of corresponding sex and age with (*a*) carcinoma of the lung, and (*b*) other forms of cancer, to calculate how many cases of previous respiratory illness would have occurred in each subgroup if both types of patients had had these same rates of attack. The total number expected for each illness was then readily obtained by summing the numbers in each subgroup. The numbers, "expected" on the basis of equality, can be compared with the histories actually recorded. To avoid bias due to any confusion between an earlier independent respiratory illness (in which our interest lay) and an illness induced by the presence of the tumour, we included in the analysis only such illnesses as had occurred at least five years before the interview. Occasionally illnesses occurring more than five years previously may have been due to a slow-growing tumour, but the number is unlikely, we think, to be important.

Questions were asked about the past occurrence of pneumonia, pulmonary tuberculosis, pleural effusion, chronic bronchitis, asthma, and chronic nasal catarrh. The results (Table XVII) show that the lung-carcinoma patients more frequently had a history of preceding pneumonia or chronic bronchitis, while other respiratory illnesses were referred to with approximately equal frequency by the two groups. The differences in the incidence of pneumonia and chronic bronchitis are statistically significant (particularly the latter), though the actual proportion of lung-carcinoma patients with positive histories is not large (with each disease 17%).

TABLE XVI.—*Exposure to Different Forms of Heating: Lung-carcinoma and Matched Control Patients. (Information obtained during part of the investigation only)*

Type of Heating in Living-room of Patients' Residence	Disease Group	No. of Patients Exposed for Different Durations of Time				Total No. of Patients	Test of Significance of Difference
		Never	1 Yr.–	30 Yrs.–	50 Yrs.+		
Coal fire	Lung carcinoma	9	93	434	735	1,271	$\chi^2=1·01$, n=3, $0·70<P<0·80$
	Other diseases	11	105	429	726	1,271	
Anthracite stove	Lung carcinoma	1,261	6	3	1	1,271	Combining all over 1 yr.:
	Other diseases	1,258	12	1	0	1,271	$\chi^2=0·39$, n=1, $0·50<P<0·70$
Gas fire	Lung carcinoma	1,192	59	13	7	1,271	Combining all over 30 yrs.:
	Other diseases	1,169	74	21	7	1,271	$\chi^2=3·25$, n=2, $0·10<P<0·20$
Electric fire	Lung carcinoma	1,184	62	14	11	1,271	Combining all over 30 yrs.:
	Other diseases	1,172	71	21	7	1,271	$\chi^2=0·84$, n=2, $0·50<P<0·70$
Radiator	Lung carcinoma	1,191	66	8	6	1,271	Combining all over 30 yrs.:
	Other diseases	1,169	85	12	5	1,271	$\chi^2=2·89$, n=2, $0·20<P<0·30$
Other heating	Lung carcinoma	1,192	55	14	10	1,271	Combining all over 30 yrs.:
	Other diseases	1,189	59	16	7	1,271	$\chi^2=0·17$, n=2, $0·90<P<0·95$

TABLE XVII.—*Frequency of Occurrence of Respiratory Illnesses in the Past History; Lung-carcinoma and Other Cancer Patients**

Type of Respiratory Illness	Lung-carcinoma Patients				Other Cancer Patients				Test of Significance of Difference
	No. of Patients	History of Illness 5 or More Years Previously			No. of Patients	History of Illness 5 or More Years Previously			
		Observed		Expected		Observed		Expected	
		No.	%	No.		No.	%	No.	
Asthma	1,465	19	1·3	19·5	853	13	1·5	12·5	$\chi^2=0·033$, n=1, 0·80<P<0·90
Chronic bronchitis	1,465	254	17·3	222·9	853	94	11·3	125·1	$\chi^2=14·13$, n=1, P<0·001
Chronic nasal catarrh	1,465	198	13·5	189·2	853	90	11·0	98·8	$\chi^2=1·35$, n=1, 0·20<P<0·30
Pleural effusion	1,465	25	1·7	25·7	853	14	1·7	13·3	$\chi^2=0·057$, n=1, 0·80<P<0·90
Pneumonia	1,465	250	17·1	224·8	853	83	10·1	108·2	$\chi^2=10·03$, n=1, P<0·01
Pulmonary tuberculosis	1,465	11	0·8	13·1	853	8	1·1	5·9	$\chi^2=1·09$, n=1, 0·20<P<0·30

* Excluding cancer patients notified incorrectly as having lung carcinoma (see Table XIX).

TABLE XVIII.—*Frequency of Occurrence of Previous Pneumonia and Chronic Bronchitis: Lung-carcinoma and Other Cancer Patients,* Subdivided by Age and Sex*

Age	Men								Women							
	Lung-carcinoma Patients				Other Cancer Patients*				Lung-carcinoma Patients				Other Cancer Patients*			
	No. of Patients	History of Illness 5 or More Years Previously			No. of Patients	History of Illness 5 or More Years Previously			No. of Patients	History of Illness 5 or More Years Previously			No. of Patients	History of Illness 5 or More Years Previously		
		Pneumonia		Chronic Bronchitis		Pneumonia		Chronic Bronchitis		Pneumonia		Chronic Bronchitis		Pneumonia		Chronic Bronchitis
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
25–	17	5	18	3	16	7	0	15	0	4	3	1	22	0	17	7	2	12	0	0
35–	116	19		18		46	8		2		15	3		3		26	2		0	
45–	493	83	17	72	15	109	15	14	11	10	38	4	11	10	26	81	4	5	5	6
55–	545	103	19	107	20	213	20	9	27	13	34	3	9	7	21	101	5	5	13	13
65–74	186	26	14	30	16	151	18	12	22	15	18	3	17	4	22	112	9	8	14	13
Total	1,357	236	—	230	—	526	61	—	62	—	108	14	—	24	—	327	22	—	32	—

* See footnote to Table XVII.

Detailed figures for the previous occurrence of these two diseases are given in Table XVIII. The lung-carcinoma patients show a uniformly higher incidence of each disease in both sexes and in all age groups, though in men many of the differences are quite small. In neither group, however, does the frequency of a past history of pneumonia increase with age as would naturally be expected. It is not unlikely that some older patients forgot their earlier attacks of pneumonia. This being so, the differences found between the lung-carcinoma and the other cancer patients may merely have arisen because patients with a respiratory disease recall more completely their previous respiratory infections—that is, for the very reason which led us to exclude other respiratory illnesses from the control group. This possibility can, however, be tested by comparing the histories given by patients thought to have carcinoma of the lung when they were interviewed but in whom the diagnosis turned out to be erroneous (Table XIX) with the histories given by the lung-carcinoma patients and by the other cancer patients (Table XVIII).

The incorrectly notified patients gave, in nearly every sex and age group, a history of previous pneumonia and chronic bronchitis of similar frequency to that given by the patients with lung carcinoma and of greater frequency than that of the patients with other forms of cancer. For all sex and age groups taken together the proportions with a positive history were:—pneumonia: incorrectly notified patients 20%, lung-carcinoma patients 17%, other cancer patients 10%; chronic bronchitis: incorrectly notified patients 21%, lung-carcinoma patients 17%, other cancer patients 11%.

When age and sex differences are allowed for (Table XIX) the incorrectly notified patients and the lung-carcinoma patients do not differ significantly, while the differences between the incorrectly notified patients and the group of other cancers are highly significant. It would seem, therefore, that the more frequent history of a preceding attack of pneumonia or of frequent attacks of chronic bronchitis in the lung-carcinoma group may well result from patients with respiratory symptoms recalling their previous attacks of certain common respiratory illnesses more readily than other patients (though it is possible that the lung-cancer and the incorrectly diagnosed groups both have suffered a greater frequency of such attacks in the past). On the present evidence we feel unable to deduce any aetiological relationship between lung carcinoma and previous respiratory illness.

TABLE XIX.—*Frequency of Occurrence of Previous Pneumonia and Chronic Bronchitis: Patients Incorrectly Thought to have Lung-carcinoma, Subdivided by Age and Sex*

Age	Patients Incorrectly Thought to have Lung Carcinoma							
	Men				Women			
	No. of Patients	History of Illness 5 or More Years Previously:			No. of Patients	History of Illness 5 or More Years Previously:		
		Pneumonia		Chronic Bronchitis		Pneumonia		Chronic Bronchitis	
		No.	%	No.	%	No.	%	No.	%
25–	17	5	25	2	14	14	1	22	5	30
35–	48	11		7		9	4		2	
45–	79	11	14	10	13	25	4	16	5	20
55–	98	25	26	25	26	15	3	20	3	20
65–74	25	3	12	9	36	5	1		1	
All ages	267	55	—	53	—	68	13	—	16	—

Comparison with patients proved to have lung carcinoma

Patients incorrectly thought to have lung carcinoma:
- No. giving a history of previous pneumonia 68
- No. expected to give such a history .. .. 59·9
  $\chi^2=1·64$, n=1, P=0·20
- No. giving a history of previous chronic bronchitis 69
- No. expected to give such a history .. .. 61·99
  $\chi^2=1·20$, n=1, 0·20<P<0·30

Comparison with other cancer patients

Patients incorrectly thought to have lung carcinoma:
- No. giving a history of previous pneumonia 68
- No. expected to give such a history .. .. 48·22
  $\chi^2=13·84$, n=1, P<0·001
- No. giving a history of previous chronic bronchitis 69
- No. expected to give such a history .. .. 44·5
  $\chi^2=21·43$, n=1, P<0·001

Validity of the Results

The larger and more detailed data that we have presented here confirm those in our preliminary report, and support our conclusion that there is an association between smoking and carcinoma of the lung. Other explanations of the figures might, however, be possible, and we carefully considered several alternatives in our earlier paper—namely, (*a*) that our group with carcinoma of the lung was unrepresentative of patients with that disease; (*b*) that the patients in the control group were not truly comparable with the lung-carcinoma patients; (*c*) that the method of selection of the control patients had led to the choice of patients who smoked less than the average; (*d*) that the lung-carcinoma patients tended, because of their disease, to exaggerate their smoking habits; (*e*) that the interviewers tended to scale up the smoking habits of the lung-carcinoma patients; and (*f*) that the individual interviewers might have obtained different results and have interviewed different proportions of the patients in the various disease groups.

The main points of the arguments that we put forward against these alternative explanations are illustrated in Table XX, which, utilizing the various groups of control patients, shows the proportions who smoked different amounts of tobacco, standardized according to the age distribution of the population of England and Wales, between the ages of 45 and 74.

In this standardization the incidence rate of smoking in a given age group in a given sample of patients was applied to the number of men—or women—in that age group in England and Wales to give the numbers of smokers in the general population. The summation of the figures thus derived from each separate sex/age group gave the total distribution in the standard population of smokers of different amounts—which were then converted into a percentage distribution as shown in Table XX. The two age groups under 45 years were omitted from the calculations because there were few such patients in some disease groups, and these unreliable figures would have been given undue weight in the process of standardization.

Table XX shows (*a*) that the lung-carcinoma group contains a smaller proportion of non-smokers and light smokers and a higher proportion of heavy smokers than *any* of the other disease groups, and (*b*) that the proportions in the group of patients incorrectly thought to have carcinoma of the lung and in the groups with other respiratory diseases, with cancer in other sites, and with other diseases, are similar. We would, as before, lay special stress upon the group of patients believed by the interviewers to have carcinoma of the lung at the time of interview, but who proved finally not to have that disease. This group reveals a distribution of smoking habits very similar to that shown by the other groups but very different from that of the lung-carcinoma patients.

TABLE XX.—*The Smoking Habits of Patients in Different Disease Groups, Standardized According to the Age Distribution of the Population of England and Wales Aged 45–74, at June 30, 1950*

Disease Group	Percentage of Non-smokers	Percentage Smoking Daily Average of				No. of Patients Interviewed Aged 45–74
		Less than 5 Cigs.	5 Cigs.–	15 Cigs.–	25 Cigs.+	
Men						
Carcinoma of lung ..	0·3	4·6	35·9	35·0	24·3	1,224
Patients incorrectly thought to have carcinoma of lung ..	5·3	9·9	35·5	37·8	11·4	202
Other respiratory diseases	1·9	9·9	38·3	38·7	11·2	301
Other cancers ..	4·6	9·4	47·2	26·0	12·8	473
Other diseases ..	5·6	9·0	44·8	26·9	13·7	875
Women						
Carcinoma of lung ..	40·6	13·7	22·0	9·5	14·2	90
Patients incorrectly thought to have carcinoma of lung ..	66·9	16·4	12·7	4·2	0·0	45
Other respiratory diseases	66·5	22·4	0·0	11·1	0·0	25
Other cancers ..	68·4	14·3	11·0	5·0	1·3	294
Other diseases ..	55·9	22·1	17·5	3·6	0·9	157

These observations make it unreasonable, we suggest, (*a*) to attribute the results to exaggeration by the lung-carcinoma patients, since patients with other respiratory diseases would presumably be equally inclined to exaggerate their smoking histories; (*b*) to attribute the results to bias on the part of the interviewers, since patients who were believed by them to have lung carcinoma but who were finally proved not to would have been recorded, had there been bias, as having smoking habits similar to the patients proved to have lung carcinoma; (*c*) to attribute the results to some special selection of control patients who were, on the average, light smokers, since there is no important difference between patients without carcinoma of the lung who were *notified* to us—that is, the incorrectly diagnosed group and the greater part of the other cancer group—and patients who were *selected* as controls by the interviewers on the basis laid down (that is, the respiratory disease group and the great majority of the "other diseases" group).

The further extensive data collected since the publication of our first report have proved to be essentially similar to the earlier data, and we have obtained no subsequent information to throw doubt on the validity of the conclusion that there is a real association between smoking and carcinoma of the lung.

Some figures for the smoking habits of the general population of Great Britain in 1951 have been obtained, for other purposes, by the Social Survey of the Central Office of Information, and it is of interest to see how these compare with the habits recorded by our hospital patients. The survey of the general population was made in May, 1951, and was based upon interviews made by trained investigators with a representative random sample of the civilian population of Great Britain aged 21 years and over. The names of persons to be interviewed were selected at random from local records in a representative sample of about 100 urban and rural local authority areas of different types throughout Great Britain. The sample thus adequately represented the population in respect of sex, age, and all other relevant factors. The questions about smoking were part of an extensive investigation concerned mainly with other subjects; they were, however, drawn up in such a way as to permit the replies to be compared with those of our inquiry.

To avoid difficulties of geographical variations in smoking habits we have limited the comparison to patients and individuals in the Social Survey sample who were resident in Greater London—from which the greater part of our data came. To eliminate differences due to variation in smoking habits with age we have taken the age distribution of the Social Survey sample as a standard and adjusted the patients to that age distribution before calculating the percentage distribution of the different grades of smokers (by, as usual, applying the incidence rates of smoking in the patients at each given age to the Social Survey population of that age and summing for the age groups). Persons of 75 and over were excluded. Table XXI shows that the percentages of non-smokers and light smokers among women agree closely, but it appears on the whole that somewhat heavier smoking habits have been recorded amongst the patients than in the sample of the general public.

Differences in the dates of the interviews (April, 1949, to February, 1952, in the one case, May, 1951, in the other) are unlikely to have influenced the results appreciably, as the national consumption of tobacco varied very little over that period. It may be argued that the differences indicate an association between smoking and many separate diseases; they may, on the other hand, result from the different methods of interviewing and from the different groups of interviewers employed. The comparison certainly provides no evidence that the association we have

TABLE XXI.—*Comparison Between Smoking Habits of Patients Without Carcinoma of the Lung, Interviewed in the Investigation, and of the General Public, Interviewed by the Social Survey Investigators; Residents in Greater London Only*

Subjects	Percentage of Non-smokers	Most Recent Amount Smoked. Percentage Smoking: 1 Cig.–	5 Cigs.–	15 Cigs.–	25 Cigs.+	No. Interviewed
Men						
Patients with diseases other than lung carcinoma	7·0	4·2	43·3	32·1	13·4	1,390*
Sample of general public (Social Survey)..	12·1	7·0	44·2	28·1	8·5	199
Women						
Patients with diseases other than lung carcinoma	54·7	13·0	21·6	8·2	2·5	456
Sample of general public (Social Survey) ..	52·9	16·9	24·3	4·7	1·2	255

* This number is three less than that shown in Table XIII, because the patients interviewed in the special investigation in rural hospitals are not included.

observed between smoking and carcinoma of the lung can be attributed to a selective choice, for comparison with the lung-carcinoma patients, of other patients who tended to be light smokers.

Discussion

In discussing the data of our preliminary report we concluded that there is a real association between carcinoma of the lung and smoking, but pointed out that this is not necessarily to say that smoking causes carcinoma of the lung. "The association would occur if carcinoma of the lung caused people to smoke or if both attributes were end-effects of a common cause. The habit of smoking was, however, invariably formed before the onset of the disease (as revealed by the production of symptoms), so that the disease cannot be held to have caused the habit; nor can we ourselves envisage any common cause likely to lead both to the development of the habit and to the development of the disease 20 to 50 years later. We therefore conclude that smoking is a factor, and an important factor, in the production of carcinoma of the lung."

Investigations in Germany (Müller, 1939; Schairer and Schöniger, 1943) and in the U.S.A. (Schrek, Baker, Ballard, and Dolgoff, 1950; Wynder and Graham, 1950; Levin, Goldstein, and Gerhardt, 1950; Mills and Porter, 1950) have led to very similar conclusions. In Britain, McConnell, Gordon, and Jones (1952) found no difference between the proportions of "non-smokers" in 100 lung-carcinoma patients and in 200 control patients (collected at a later date). On the other hand, they showed a considerable difference among cigarette-smokers between the proportions smoking the larger quantities: 44.1% of the lung-carcinoma group had smoked more than 20 cigarettes a day against 23.2% of the controls.

The present analysis of nearly 1,500 cases, or more than double the number dealt with in our preliminary report, supports the conclusion then reached and has revealed no alternative explanation—for example, in the use of petrol lighters.

It has been suggested that subjects with a particular physical constitution may be prone to develop (*a*) the habit of smoking and (*b*) carcinoma of the lung, and that the association might therefore be indirect rather than causal (Parnell, 1951). We know of no evidence of such a physical constitution characteristic of patients with lung carcinoma. If it does exist we should still have to find some environmental factor to account for the increased incidence of the disease in recent years.

To say that smoking is a factor in the production of carcinoma of the lung is not, of course, to say that it contributes to the development of *all* cases of the disease. All observers agree that the disease occurs in non-smokers, and in the present series there were 34 such cases confidently diagnosed and histologically proved. These 5 men and 29 women said that they had never smoked at all or had smoked so little as never to have consumed as much as one cigarette a day for as long as one year. Such patients in the ordinary course of their lives must have inspired air containing tobacco smoke, and it is not possible to say whether the disease would occur in its complete absence. The reasonable presumption is that it would. Experience of cancer in other sites (for example, cancer of the skin) indicates that it is unlikely for one environmental agent to be the effective cause in all cases.

Whether smoking is the sole cause of the *increase* in the disease in recent years is another matter. There is no evidence to show whether there has been an increased incidence among non-smokers. It is certain, we think, that some, if not much, of the increase is spurious and merely the result of improved diagnosis. Rigdon and Kirchoff (1952) have pointed out that in the U.S.A. the death rate attributed to lung cancer in the different States is positively correlated with the number of physicians per 1,000 inhabitants, and it can be shown, from their figures, that this is true independently of the correlation with cigarette consumption—which is also related to the number of physicians per 1,000 inhabitants. The extent to which the increase is real does not, however, affect the present evidence from which the association between smoking and lung carcinoma is deduced. It would be material if it were proved that there had, in fact, been *no* true increase of the disease following a great increase in the consumption of tobacco; but that, in our opinion, is as far from having been proved as that the recorded increase is all real. The position, then, as we see it, is (*a*) that an association has been demonstrated—here and elsewhere—between tobacco-smoking and carcinoma of the lung; (*b*) that, independently of this evidence, there has been a recorded increase over the years in the number of deaths attributed to the disease and an increase has also occurred in the consumption of tobacco, and particularly of cigarettes; (*c*) that the increase in the number of deaths recorded is relatively greater than the increase in the consumption of tobacco, but the actual relation between the real increase in the number of deaths and the increase in the consumption of tobacco is entirely a matter of conjecture.

Needless to say, environmental factors other than tobacco may be responsible for part of the presumed increase. The part played by any such factors cannot, however, be deduced merely from a contemporaneous increase in their incidence and in the death rate from lung cancer—that is, on the basis of a correlation in time: a direct association between the disease and exposure to them must be demonstrated. In the present investigation some additional, but not very strong, evidence was obtained that lung carcinoma is commoner in urban than in rural areas, but otherwise we found no major or clear association apart from that with the consumption of tobacco.

We should perhaps point out that we made no inquiries which would throw light upon a relationship between the development of lung carcinoma and an attack of influenza during the pandemic of 1918–19—a relationship from time to time suggested in the literature (see *Lancet*, 1951, **2**, 737). It would be difficult to gather sufficiently accurate information on such a disease after the passage of so many years. We may note (*a*) that no appreciable increase in lung cancer has occurred in Iceland (Dungal, 1950), though the influenza pandemic was severe there, and (*b*) that, in Britain, influenza in 1918–19 affected both sexes almost equally (as judged by mortality), while deaths from lung cancer occur predominantly in men.

Year	Influenza (Death Rate per Million) M	F	Year	Lung Cancer (Death Rate per Million) M	F
1918	3,360	2,967	1948	422	83
1919	1,350	1,101	1949	453	86

All methods of smoking tobacco do not, according to our results, carry equal risks. As in our previous report, smoking a pipe appears to be less closely associated with the disease than smoking cigarettes. In the present observations we have found that, contrasted with other patients, rather fewer of the patients with carcinoma of the lung have used a cigarette-holder or smoked filter-tipped cigarettes. These observations are of interest, though it is impossible to draw any firm conclusions from them since so few people have limited themselves throughout their lives to one method of smoking. It must also be remembered that any smoking technique which is differentially associated with a tendency to light smoking will necessarily, according to our figures, appear to be less closely related to lung carcinoma. Nevertheless, it seems possible, from these results, that pipes, cigarette-holders, and filter tips may, to some unknown extent, each partly separate out an active agent before it reaches the respiratory tract.

On the other hand, the observation that patients who recognize that they inhale are found no more frequently in the lung-carcinoma group than in the control group appears somewhat paradoxical. We pointed out, however, in our preliminary report that until the size of the particles carrying the carcinogen is determined nothing can be stated about the effect which differences in depth of respiration may have on the extent and site of deposition of the carcinogen. From the present extended observations it seems that patients with growths of central origin inhale less frequently than normal (though the difference is very small), while patients with peripheral growths may inhale rather more frequently. Such a finding could be expected if smoke when not "inhaled" were to penetrate mainly to the large bronchi while inhaling spread the deposition of smoke particles more evenly throughout the bronchial tree.

From the evidence collected about each patient's smoking habits it has been possible to compute some estimates of the risks of dying from carcinoma of the lung in different age groups at different levels of tobacco consumption. These estimates, we would emphasize, are speculative and dependent on the validity of three assumptions: namely, first, that the smoking habits of the lung-carcinoma patients interviewed in this inquiry and resident in Greater London are representative of the habits of all persons dying of the disease in Greater London in 1950; secondly, that the smoking habits of the patients with other diseases interviewed in this inquiry and residents of Greater London are representative of the habits of the general population of Greater London in 1950; and, thirdly, that the actual numbers of deaths from carcinoma of the lung in each sex in Greater London were close to the numbers recorded by the Registrar-General. The only one of these assumptions upon which we have a check is the second. Observations on smoking habits made by the Social Survey upon a cross-section of inhabitants of Greater London do not differ radically from the observations based upon our patients, though they reveal rather fewer heavy smokers than we have found. Keeping these assumptions in mind, our estimates indicate that the risk of dying of lung carcinoma increases with age, as is of course known, and in approximately simple arithmetical proportion with the amount smoked.

A test of the truth of this conclusion is to see whether it accords with the observed incidences of lung carcinoma and of tobacco consumption in different sections of the community and in different parts of the world. In this country there is a pronounced difference in the smoking habits of men and women; it appears inadequate to account for the whole excess of cases which occur in men, as is shown by the different death rates estimated for each sex at each level of tobacco consumption (Table XII and the Figure, based upon it). On the other hand, the sex ratio of the relatively few cases observed in non-smokers is not incompatible with a similar incidence in men and women in the absence of smoking—it could not be identical because of risks associated with certain industrial occupations. There is also an appreciable difference in smoking habits between men living in town and country, which should lead to a higher death rate in the towns, but not to the extent that is actually observed.

It may be that other factors also operate to produce these different death rates in men and in women, in towns and in the countryside. On the other hand, the relationship between smoking and lung carcinoma is quite likely to be more complex than that depicted in Table XII. For example, common observation would suggest that some women—especially the light smokers among them—tend to hold their cigarettes in their mouths less continuously than men and not to smoke them to the end. An equal number of cigarettes a day may not therefore be the same thing, from the point of view of cancer risk, when smoked by men and by women. Again, differences in consumption of cigarettes in town and country may have been more pronounced 10 or 20 years ago than they are to-day. We have no information to guide us.

Stocks (1952) has, however, shown a distinct relation between the size of a town—assessed by the number of occupied dwellings—and the mortality from lung cancer. It would seem likely that some agent other than tobacco (present perhaps in domestic chimney smoke or in the exhaust fumes of cars) is at least partly responsible for the excess mortality in towns.

Comparisons between the recorded death rates at different epochs and in different countries present many difficulties in interpretation. Varying standards of diagnosis of the cause of death, differences in methods of preparation and consumption of tobacco, changes in consumption over the last 50 years, may all introduce gross errors. Nevertheless, some correlation between national figures for cigarette consumption and the death rate from lung cancer would be expected, though in view of the uncertainties of the data the correlation is unlikely to be high. Studying the incidence of lung cancer in some European countries, Daff, Doll, and Kennaway (1951) conclude: "The consumption of tobacco per head has been for the last 10 years rather higher in Switzerland than in the United Kingdom, and in Norway has been about one-half that in the other two countries, while the crude death rates at the beginning and end of the period were roughly in the proportion of 10 (England and Wales) to 5 (Switzerland) and 2 (Norway). Cigarette consumption was approximately in the proportion of 4 (England and Wales) to 2 (Switzerland) and 1 (Norway), and was more in accord with the relative death rates. The increase in the number of deaths has been about the same (twofold) in all three countries, but the increase in consumption of tobacco and cigarettes has been less. The differences in the incidence of cancer of the lung are therefore quite different in extent from those in the quantity of tobacco consumed; they are more like (though still different from) those in the quantity of cigarettes consumed. The study of the relation between the national consumption of tobacco and the national incidence of cancer of the lung has scarcely begun."

No responsible agent in tobacco smoke has been detected. The suggestion that arsenic, introduced by insecticides sprayed on the growing crop, might be a factor would seem to be discountenanced by the absence of arsenic from Turkish tobacco and the high proportion of lung carcinoma found at necropsy in Istanbul (Daff, Doll, and Kennaway, 1951; Saglam, 1944). Benzpyrene has not been detected in cigarette smoke (Waller, 1952). Long-continued exposure of mice to atmospheres containing tobacco smoke has failed to produce lung cancer (Campbell, 1936; Lorenz, Stewart, Daniel, and Nelson, 1943), but it may be of significance, in view of our findings, that the smoke was brought to the mice through long tubes. In contrast, tumours of the skin of mice can be produced by the application of tars obtained from tobacco burnt at temperatures which occur in normal smoking (Lamb and Sanders, 1932; Flory, 1941). Goulden, Kennaway, and Urquhart (1952) have pointed out that carcinogenic agents

in tobacco smoke and in town dust might supplement one another, and have summarized the available data about the additive effects of two carcinogens. An agent in tobacco smoke might be by itself only weakly, if at all, carcinogenic, but might act as a co-carcinogen in the presence of, for example, the benzpyrene in urban atmospheres.

Summary

In an investigation designed to throw light on the aetiology of carcinoma of the lung nearly 5,000 hospital patients have been interviewed by four specially appointed almoners. The interviews took place in the years 1948 to 1952 in hospitals in London, Bristol, Cambridge, Leeds, Newcastle-upon-Tyne, and (for a limited purpose) in the rural areas of Dorset and Wiltshire. The questions asked covered a very wide range, including the occupational histories of the patients, where they had lived and the forms of domestic heating in their homes, their previous attacks of respiratory illnesses, their habits with regard to smoking, and, for other purposes, some particulars of their dietary habits and use of purgatives.

Preliminary figures on tobacco-smoking were published in a previous paper (Doll and Hill, 1950). The present paper gives corresponding data for the whole of the material collected as well as the analysis of other questions included in the inquiry. The main comparisons are between 1,465 patients with carcinoma of the lung and an equal number of "matched control" patients with other diseases, each of these being carefully chosen so as to be of the same age, the same sex, and, so far as possible, in the same hospital at the same time as a lung-carcinoma patient.

There is no appreciable difference between the two groups in the number of persons belonging to the Registrar-General's five social classes, and no association has been found between any type of occupation and lung carcinoma which would suggest the presence of an aetiological agent likely to be of general significance.

With regard to the possible effects of fumes in the atmosphere, both within and without the home, there is no significant difference between the groups. Of the lung-carcinoma patients 23.0%, and of the control patients 21.5%, had lived near a gasworks for a year or more. Their use of coal, gas, or electric fires or other forms of heating in the living-rooms of their homes did not differ appreciably.

In conformity with the national death rates rather fewer of the lung-carcinoma patients lived, or had lived, in the countryside and more, correspondingly, in the towns.

The lung-carcinoma group in comparison with patients with other forms of cancer more often gave a history of a previous attack of pneumonia and of chronic bronchitis. Detailed analysis of the data suggests, however, that this difference may be due merely to the lung-carcinoma patients, with their respiratory symptoms, recalling more readily than other persons their previous attacks of respiratory illness. The data are not accurate enough for an aetiological relationship to be postulated.

Of the 1,357 men with carcinoma of the lung 7, or 0.5%, were non-smokers (as defined in the text); of the 108 women there were 40, or 37.0%. The corresponding figures for their paired controls were 61 men (4.5%) and 59 women (54.6%). Of the men with lung carcinoma 25.0% reported that they had been smoking, before the onset of their illness, an average of 25 or more cigarettes a day (or the equivalent in pipe tobacco). The corresponding figure for the male control patients was only 13.4%. For women these proportions were 11.1% for the carcinoma group and 0.9% for the controls.

For men these differences are present consistently in each of the five areas of inquiry. For women they are present in London but not in the 28 patients observed in the provincial towns, where only one woman with the heavier smoking habits was found.

Estimated death rates for Greater London (on assumptions stated in the text) indicate that the mortality from carcinoma of the lung may increase in approximately simple proportion with the amount smoked. Amongst men of ages 45–64 the death rate in non-smokers is negligible, while in the heavier-smoking categories it is estimated to reach 3 to 5 deaths per annum per 1,000 living.

Regular users of petrol lighters were found with equal frequency in patients with lung carcinoma and in the control patients with other diseases (42.9% and 41.3%); the proportions who said they inhaled were similar (64.6% and 66.6%); and so were the proportions of cigarette-smokers who had smoked mainly hand-rolled cigarettes (20.7% and 19.1%). On the other hand, rather fewer of the cigarette-smoking patients with lung carcinoma had ever used a cigarette-holder regularly (5% against 12% of the controls), and only 3 out of 504 had smoked filter-tipped cigarettes, compared with 15 out of 467 controls. The observations in these respects are too few for a definite conclusion, but conceivably they may have a bearing on the appreciably lower risks reported here for pipe-smokers compared with cigarette-smokers. Each of these methods of smoking might partly separate out an active agent before it reached the respiratory tract.

The validity of these various results is studied, and it is concluded that the association between smoking and carcinoma of the lung is real. It is not argued that tobacco smoke contributes to the development of all cases of the disease—a most unlikely event. It is not argued that it is the sole cause of the increased death rate of recent years nor that it can wholly explain the different mortality rates between town and country.

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The centenary of the birth of Antoine Henri Becquerel, the French physicist, falls on December 15. Like his father and grandfather before him, he occupied the chair of physics at the Musée d'Histoire Naturelle, Paris, to which he was appointed in 1892. Three years later he became professor of physics at the Ecole Polytechnique. In 1896 he made the discovery that uranium ores at ordinary temperatures emit an invisible radiation similar in several respects to *x* rays, and capable of fogging a photographic plate after passing through metal plates. Pierre and Marie Curie investigated this radiation and showed it to be an atomic phenomenon. They named it radioactivity. The discovery of radium by the Curies followed in 1898, and they shared the Nobel Prize for Physics with Becquerel in 1903. Becquerel also made important contributions to the knowledge of magnetism, polarization of light, phosphorescence, and absorption of light in crystals. He died at Croisic, Brittany, on August 25, 1908.

PSYCHIATRIC DISORDERS IN LATER LIFE*

BY

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"Grow old along with me!
The best is yet to be,
The last of life, for which the first was made:"

As Robert Browning's words imply, it is probable that psychogenic factors causing simple anxiety and hysterical reactions play less part in later life than they do at earlier ages. But, as Sir Humphry Rolleston remarked, quoting another authority: "Whatever may be said in favour of it, old age is a losing game." There is the high incidence of cerebral vascular disease, and intracranial tumours occur with some frequency. Affective disturbances are common. But I should like to refer chiefly to the two principal organic syndromes seen in later life: the syndrome of acute clouding of consciousness, delirium, or confusion, and that of presenile dementia. There is particularly the relation of the former to biochemical and toxic factors and of the latter to intracranial disease.

1. Biochemical and Toxic Causes of Psychiatric Symptoms in Later Life

Great as are the differences between the age periods of growth and decline, both the very young and the very old show an undue mental instability in response to disturbances in their body chemistry. Thus, an elderly person who exhibits at the most only slight mental signs of ageing, may, through the fortuitous introduction of a biochemical or toxic factor, develop acute mental symptoms indicative of clouding of consciousness. In increasing order of severity these are: (1) Simple impairment of attention, registration, and recall, often associated with a facile or euphoric affect and push of talk. (2) Perseveration showing itself in the spontaneous behaviour, in the speech, and in the response to simple requests. (3) Disorientation in time, place, and for persons, usually at some stage with confabulation. In many instances, concrete orientation may be correct or the time sense only lost, but further testing will reveal evidence of abstract disorientation. (4) In more severe cases there are grossly defective grasp and delirium with noisy and irrational behaviour.

Recognized causes of such (usually reversible) effects are toxaemia from fever or urinary infection; the incautious use of bromides, morphine, barbiturates, or other drugs; and vitamin deficiency. Other causes which, although known, are less generally appreciated include dehydration, alkalosis, anoxia, and hypoglycaemia.

Dehydration

If a sufficient fluid intake is not secured dehydration will arise in any feverish condition or after a surgical operation (such as prostatectomy) requiring general anaesthesia. The statement that the patient has "passed urine" has little weight in this respect unless it is known that the output is adequate and the specific gravity satisfactory. The after-care of old people undergoing operation for cataract also deserves note. Hallucinations and disorientation or acute delirium may occur as the result of a combination of unfavourable circumstances such as recumbency, bandaging

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of the eyes, and the use of atropine locally or of other drugs such as barbiturates and morphine administered for their sedative effect. Which of these factors is chiefly responsible in patients who develop mental symptoms it is difficult to say, but I think the role of dehydration is important, as is that of the routine use of sedative drugs. Vomiting is not an infrequent post-operative complication, and awareness of this and of the need to encourage rest may lead to the inadvertent restriction of fluid. Similarly, if it happens that the nurse is not present when the patient awakes from sleep, his agitation at finding he cannot see may induce over-breathing, which may be harmful when added to the other factors. My ophthalmological colleague, Mrs. Beatrice Lynn, has kindly furnished me with the notes of three such cases which she has seen this year. One of these is recorded below.

A man aged 82 had mental symptoms the day after operation, when he became disorientated and restless, and later was noisy and difficult to keep in bed. Phenobarbitone sodium and pethidine had no calming influence and his tongue was very dry. Fluids were given freely and the double bandages removed, only the operated eye being kept covered. On the fourth day, however, the mental state still continued to be abnormal; there were some indications of bronchopneumonia and penicillin was ordered. Notwithstanding his stormy passage, the eye did very well and within seven to eight days the acute mental symptoms had subsided. He was subsequently discharged from hospital in good health.

Alkalosis

Vomiting and overbreathing from any cause or the excessive intake of alkalis—for example, in combating urinary infections and in hypochondriacs—may induce alkalosis, the altered *p*H of the blood interfering with the dissociation of oxyhaemoglobin so that cerebral cortical function is disturbed, if not to the same extent at least in the same way as in anoxia. The mode in which adverse toxic and biochemical effects may build up before suddenly giving rise to mental symptoms is illustrated in the following case.

An alcoholic aged 59 had emphysema, the result of a life-long tendency to asthma. He was admitted for treatment, but in view of his poor physical condition was allowed the usual quantity of alcohol. Vitamin B_1 was given daily intramuscularly. There was occasional vomiting and he had a bout of diarrhoea. After a week, during which the mental state showed no gross abnormality, he had a severe paroxysm of asthma for which ¼ gr. (16 mg.) of morphine was given, the same dose being repeated 12 hours later. Then quite suddenly he became hallucinated and deluded, insisting that he was being observed by men looking down from a hole in the ceiling, that the walls of the room were brightly coloured, and that the medical and nursing staff were in conspiracy against him. Within 48 hours, probably assisted by glucose and insulin, he had recovered.

Cerebral Anoxia

This is a more serious danger than any of the above, especially in later life. It may result from sudden severe haemorrhage or during surgical operations when difficulty arises with the anaesthetic. Modern methods both of anaesthesia and of blood replacement have not entirely eliminated this risk, which I think should be more widely recognized. The following case is an example.

A man aged 58 had a previous history of duodenal ulcer with repeated severe haematemesis and melaena, requiring blood transfusion. He was first seen five years later on account of "nervousness," which meant that in the previous six months hesitancy in speech and increasing absentmindedness had been observed. On examination he was peevish and suspicious, though otherwise indifferent to his state. His talk was circumstantial. Paraphasia often occurred, and he had difficulty in recalling proper names. Perseveration was pronounced. He was disorientated, and the attention was difficult to sustain. He was unable to register an address except with great difficulty and he had completely forgotten it a few minutes later. The blood pressure was normal and there were no neurological signs. The Wassermann reaction was negative and except for some increase of protein and a trace of globulin the cerebrospinal fluid was normal. Electroencephalography showed much theta and occasional delta activity in a generally high amplitude record, but no focus. *X*-ray films showed a grossly deformed duodenal cap and the faeces contained occult blood. Air pictures were not made at the time, but lumbar encephalography was carried out later. This showed only symmetrical dilatation of the lateral ventricles.

It is not suggested that such sequelae are common. I have seen only a few cases, but feel that attention should be directed to them. As a rule, however, it is remarkable how well persons in later life recover from even severe anoxic experiences. Thus in a series of cases of coal-gas poisoning there was one old lady of 70 who was found in bed in a gas-filled room in deep coma beside her dead husband. Over two months elapsed before she had fully recovered consciousness, yet she lived for two years and showed at the time of her death from pneumonia no evidence of deterioration.

Hypoglycaemia

Repeated hypoglycaemia occurring in elderly diabetics disturbs cerebral function very similarly to anoxia. Many of these elderly diabetics are of stout build and receive fairly large doses of insulin. It would seem advisable to treat them by restricting the total calories and reducing the insulin. Too much insistence on maintaining the blood sugar at levels of 100–150 mg. per 100 ml. leads to the appearance of mental symptoms referable to recurring hypoglycaemia. The following is the worst case of this kind I have seen.

A woman aged 62 had been taking insulin for 15 years on account of well-established diabetes, though both the dosage of insulin and the dieting had been irregular. She had had repeated hypoglycaemic reactions and her family had noticed increasing forgetfulness in the intervals. On admission to hospital the blood sugar was low, but, as the level fluctuated and she had ketosis, insulin was continued. Although apparently wakeful, she ignored the examiner, sucked her lips, picked at her tongue, and rummaged beneath the bedclothes. There was a jargon aphasia and perseveration was pronounced. Insulin was stopped and she slowly improved, although for days a paranoid mood of general suspicion persisted. After three weeks insulin was again given because of a sharp rise in the blood sugar and ketosis. She kept well for a time, but then fluctuations in the blood sugar were observed, and she passed into deep coma and died

In this case it was puzzling that the cerebrospinal fluid contained a trace of globulin and 100 mg. of protein per 100 ml. The possibility of a chronic subdural haematoma was naturally considered, but no clot was found. At necropsy the brain and meninges had a normal appearance; there was no evidence of gross cortical atrophy. On histological examination there were insufficient structural changes to account for death, which appeared to be related to the severe and recurring hypoglycaemia.

2. Mental Symptoms in Cerebral Tumour and Cerebral Vascular Accidents

It is not possible to name all the diseases of later life which disturb mental function, such as myxoedema, pernicious anaemia, disseminated sclerosis, and general paralysis. The grandiose delusions so characteristic of the last-named disease in the nineteenth century may not be so apparent in these stringent times. But the fact that this feature still has some diagnostic value is shown by the example of a little man of 58 who eked out a living by selling small quantities of coal and firebricks to his equally penurious neighbours. His disease was diagnosed after he offered his customers, all and sundry, free supplies of coal. Although one expects a positive Wassermann reaction I have seen the case of an elderly man in whom the blood was repeatedly negative, and it was not until the cerebrospinal fluid was examined that the typical findings brought the truth to light. But the chief difficulty in differentiating idiopathic presenile dementia lies in the exclusion of a tumour, and this, I think, is because of three principal reasons.

(1) The tumour, not uncommonly a meningioma, may give rise to symptoms the pattern of which may be so stealthy in its mode of unfolding or so like the attributes of

"growing old" as to escape recognition. I refer, of course, to impairment of memory, difficulty in sustaining attention and grasp, rigidity of conception, and increased mental fatigue. One may even recognize in the pattern of such symptoms the thinly veiled efforts of the patient to compensate for them, though, as Goldstein has pointed out, the degree of adaptation possible depends on the severity and rate of progress of the intellectual defects. In *chronic subdural haematoma* the falling off in intellect is more recent and more obvious to the patient's relatives, and there is the extraordinary variability in the clinical picture which makes one often doubt one's original "hunch." A history of head injury is seldom forthcoming, but acute confusional episodes are not uncommon, and a Korsakoff picture or noisy behaviour may be the principal feature when the patient is first seen.

(2) There is the relative infrequency of headache and papilloedema, circumstances no doubt related to the natural process of ageing, causing cerebral atrophy and vascular changes. The absence of headache is particularly important, and is illustrated in the following case.

The patient, a countryman aged 65, was naturally taciturn. His relatives, knowing this, had not remarked on the feature (which was very pronounced) or on his increasing absentmindedness until one day he decided to go to Belfast to do some business. He travelled by bus, and in his own words it was not until he reached the city and found "all the public houses closed" that he realized it was a Sunday. This man denied ever having had headache, though he admitted a falling away in mental energy. In the previous month he had noticed some increasing weakness in the left arm, but had attributed this to an old war wound. A meningioma the size of a small plum was found at the right frontal pole.

Headache may be inconspicuous or absent in patients in later life with an acoustic neuroma in which the deafness and ataxia may not be remarked, the gradual "knocking-off" in cerebration being more apparent.

(3) The third reason why a tumour may be overlooked in later life is because of misconceptions regarding the natural course of events in *cerebral vascular accidents* such as cerebral thrombosis. It should be more emphasized that the subsequent development of symptoms pointing to progressive mental deterioration usually forms no part of the picture, which is essentially one of greatest disturbance at the onset and gradual recession thereafter. Such symptoms in later years, with or without slowly developing hemiplegia, usually indicate tumour metastases or a primary malignant cerebral growth. There is an important point about minor vascular accidents involving the temporo-parietal or parieto-occipital regions. These often mimic simple acute confusional reactions, because there is no hemiplegia and the disturbance of speech function in dominant hemisphere lesions may be so slight as to escape recognition. The only distinct clue at first may be the finding of a contralateral visual-field defect, and this is easily overlooked because the patient is so inattentive as to make testing the fields by confrontation impossible. But if a large or brightly coloured object is projected from behind by an assistant into each half-field in turn, the readiness with which the patient's gaze is distracted to the object will usually indicate a defect if such is present.

Simple Dementia

Simple dementia is usually diagnosed in old people when there is evidence of global intellectual deterioration with amnesia as the chief feature. One thinks of cerebral vascular disease, tumour, or a special variety of dementia such as Pick's disease when there are focal signs such as dysphasia, dyspraxia, or gnostic difficulties, or a positive family history. From a practical point of view this reasoning has obvious advantages, for, although the apparent absence of focal signs does not exclude a tumour, the presence of such should rightly call attention to the possibility of some such cause which it may be possible to relieve. But from the theoretical aspect it raises the question of where one is to draw the line as regards focal signs. There can be little doubt about the significance of hemiplegia, hemianopsia, or a speech defect, but spatial and right-left bodily disorientation, visual and finger agnosia, ideational and constructional apraxia, anosognosia, and disorders of the body image lie on the borderline between neurology and psychiatry, and their significance is always difficult to assess.

I have been interested to find that many patients in later life with presenile dementia show abstract spatial disorientation of the same kind as one finds during the later phases of clouding of consciousness in cerebral vascular accidents and in cases of post-traumatic and post-anoxic encephalopathy. Drawing tests or asking the patient to indicate the situation of important towns on a map have value in detecting this, and, incidentally, such patients' drawings often resemble those of young children. Thus when drawing a house they usually represent the walls as a square or oblong with chimneys on top so as to give perspective, but the door may be drawn half-way up one side of the house and the windows be placed against the side walls. Many of these patients, like young children, seem to be unable to represent objects as they would appear when viewed from a particular vantage-point. Instead, they indicate the components without regard to their orientation, so that the result may represent a compromise between what is seen in different planes —for example, the one vertical and the other horizontal.

Other Parietal Signs

As regards the other "parietal" signs, Gerstmann's syndrome is associated with focal lesions involving the left angular gyrus and more elaborate disturbances in the body image with posteriorly placed right-sided (non-dominant hemisphere) lesions. But cases illustrating exceptions to these rules have been reported, and, as Critchley has remarked, "many of these parietal hallmarks are at times produced by lesions remote from the parietal lobe." Krynauw, too, found that hemispherectomy caused no spatial disorientation or disturbance of the body image. It appears unlikely, therefore, that they can be explained entirely on a focal basis. As with spatial disorientation, I have found them not uncommonly in idiopathic dementia during phases of confusion and in cases of post-anoxic encephalopathy with delayed recovery of full consciousness. The point about the latter, however, is that the signs—for example, right-left disorientation, finger agnosia, etc.—disappear as full consciousness is regained. The same feature may sometimes be observed in patients with extensive vascular lesions.

A woman in the late fifties had a stroke and developed left-sided hemiplegia, hemianaesthesia, and hemianopsia. Recovery to full consciousness was slow, and during the later phases there was anosognosia for the paralysed left side and pronounced disturbance in the body image. When she was asked to show her left arm she held up the right, and when the left arm was supported and brought into her restricted visual field she denied it was her own. On one occasion she was heard asking the nurse to "take it away," and from what she said it seemed evident that she was under the impression the paralysed left arm was a baby. When she was asked to point to the left arm she always pointed to a spot some distance away from it, towards the left side. She could point correctly to the left ear and nose, but at times when asked to indicate the left eye she pointed to the right. Although there appeared to be autotopagnosia for the left arm (and to a less extent for the left leg), she always knew the right side from the left and was able to indentify fingers, although in the case of the left hand she denied they were her own. In addition she denied the existence of any paralysis, and when asked why she was in hospital said it was because she "had a cold." Two months later these symptoms had disappeared. She recognized the left arm and that it was paralysed, although the sensory loss, hemiplegia, and left-sided hemianopsia persisted and her mood was fatuous and euphoric.

It is admitted that she may have recovered some sensation on the left side, enough to enable her to complete her body image, but I doubt if this is the whole answer. My impression is that these so-called parietal signs depend as much for their occurrence on the coexistence of general

clouding of consciousness as they do on the presence of an actual focal lesion in the parietal area or elsewhere in the brain.

Summary

In later life, among the reversible toxic and biochemical causes apt to provoke confusional symptoms, dehydration, alkalosis, anoxia, and hypoglycaemia deserve particular emphasis. Anoxia or repeated hypoglycaemia may lead to ultimate dementia, although as a rule only reversible acute symptoms result.

Cerebral tumour in the elderly may be overlooked because the symptoms simply resemble those of growing old, because headache and papilloedema are absent, and because progressive intellectual deterioration may be wrongly attributed to cerebral softening from vascular disease.

Parieto-occipital and parieto-temporal vascular lesions especially give rise to clinical pictures resembling post-traumatic psychosis and post-anoxic encephalopathy. The occurrence of so-called parietal signs is closely related to general clouding of consciousness, some indications of which are usually present.

TESTOSTERONE THERAPY FOR THE PRURITUS OF OBSTRUCTIVE JAUNDICE

BY

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Pruritus is a most distressing symptom in obstructive jaundice and its treatment has hitherto been very unsatisfactory. Methyltestosterone has been successfully used to relieve this symptom in two patients suffering from primary biliary cirrhosis with intrahepatic obstruction to bile flow (Ahrens *et al.*, 1950). We have extended these observations and have used methyltestosterone to treat chronic pruritus in seven patients suffering from obstructive jaundice.

Selection of Cases.—All the patients had chronic jaundice of obstructive type. Three suffered from primary biliary cirrhosis, two from inoperable carcinoma of the main hepatic ducts, one from a gall-stone impacted in the common bile duct, and one from a traumatic stricture of the common bile duct. All the patients spontaneously complained of itching and showed excoriations on the skin due to scratching. Patients with other skin diseases were excluded from this study. Pruritus had lasted for at least six weeks.

Case Reports

Case 1.—A 54-year-old woman with primary biliary cirrhosis began to have itching of the palms in June, 1950, followed by jaundice which had persisted. Examination showed skin xanthomas and hepatosplenomegaly. The faeces were usually pale but occasionally contained bile pigment. Laparotomy showed no obstruction to the extrahepatic biliary system. Pruritus increased, and by December was interfering with her sleep and making her life miserable. Phenolic skin lotions, antihistaminic drugs, and phenobarbitone were ineffective in controlling the itching. In July, 1951, she was started on methyltestosterone, 25 mg. daily sublingually. After one week's treatment she reported great relief of the itching, which completely disappeared after one month. The drug was continued for three months and the pruritus did not recur. In October sublingual therapy was replaced by a subcutaneous implant of 450 mg. of testosterone propionate. Pruritus returned within seven days and within one month was as severe as before the treatment started in July. Sublingual methyltestosterone in 25-mg. daily dosage again relieved the itching, and the drug has been continued to May, 1952.

Case 2.—A 54-year-old accountant with primary biliary cirrhosis first had jaundice in September, 1948, which has persisted. In December pruritus became troublesome. Examination showed skin xanthomas and gross hepatosplenomegaly. The stools were usually pale. The urine contained both urobilin and bilirubin. Laparotomy revealed no extrahepatic biliary obstruction. Pruritus was intractable and unaffected by phenolic lotions, antihistaminic drugs, or phenobarbitone. In December, 1951, a daily sublingual dose of 25 mg. of methyltestosterone was started and within five days the itching was less. Sublingual therapy was continued for three months and the pruritus did not recur. In March, 1952, oral therapy was stopped and 600 mg. of testosterone propionate in pellets was implanted subcutaneously. For two months the antipruritic effect was excellent, but it gradually became less effective in the third and fourth months after implantation. The pellets were then removed and weighed: 495 mg. of testosterone propionate had been absorbed in 127 days. Sublingual therapy with 25 mg. of methyltestosterone daily was then resumed, and this successfully controlled the pruritus for the succeeding two months.

Case 3.—A 69-year-old woman with an inoperable carcinoma of the hepatic common duct began to have progressive jaundice, pruritus, and loss of weight in November, 1951. Examination showed deep jaundice and gross enlargement of the liver. The stools were constantly acholic and the urine did not contain urobilin. Surgical exploration showed a primary neoplasm of the common hepatic duct, causing complete obstruction to bile flow. The patient was treated daily for eight days with linguets identical in shape, size, and taste with those containing methyltestosterone, but having no active substance. These inert "dummy" tablets had no effect on the itching. Methyltestosterone tablets were then substituted, and pruritus was relieved in six days; it recurred five days after stopping the testosterone. The patient was questioned about the pruritus by a physician who had no knowledge whether or not an active tablet was being given.

Case 4.—A 79-year-old woman with carcinoma of the main hepatic ducts developed rapidly progressive painless jaundice with pruritus in January, 1951. The liver was enlarged, the stools were usually pale, and the urine contained both urobilin and bilirubin. Phenobarbitone, antihistaminic drugs, and the local application of a phenol-containing lotion did not relieve the pruritus. In November she was started on sublingual methyltestosterone, 25 mg. daily. In six days the itching was completely relieved. On stopping the drug, the pruritus returned in three days and was allowed to become severe before sublingual methyltestosterone was again given, with further relief of the symptoms. In January, 1952, sublingual therapy was stopped and a subcutaneous implant of 450 mg. of testosterone propionate given. This was ineffective in controlling the itching, which returned in six days. Thirty-three days after the insertion the implant was removed and only 56.9 mg. had been absorbed. Sublingual testosterone treatment was once more effective. Intramuscular testosterone propionate in a dose of 25 mg. twice a day was tried, but proved of little, if any, value in controlling the pruritus. The patient died in April, and necropsy showed a carcinoma of the main hepatic ducts in the porta hepatis.

Case 5.—A 45-year-old woman, with a gall-stone in the common bile duct, began to have upper epigastric pain, nausea, and vomiting six weeks previous to admission. Jaundice and pruritus quickly followed, and the jaundice progressively deepened. Examination showed only hepatomegaly; the gall-bladder was not palpable or tender. The faeces were acholic. The urine showed bilirubin and a persistent absence of urobilin. Control pharmacologically inert linguets were started, and seven days later the pruritus was still very distressing to the patient. The inert linguets were then replaced by daily sublingual administration of a tablet containing 25 mg. of methyltestosterone. Within four days the itching was much less severe, and seven days after starting the drug pruritus had ceased. Operation showed a gall-stone impacted in the lower end of the common bile duct.

Case 6.—A 41-year-old woman with primary biliary cirrhosis started to have skin irritation in November, 1950. Although the urine was dark in colour jaundice was not noticed until December, 1951. Examination showed hepatosplenomegaly. The faeces varied in colour, and, although usually acholic, occasionally their colour was almost normal. Urine contained urobilin and bilirubin. Laparotomy failed to demonstrate any extrahepatic biliary obstruction. Pruritus continued severe and persistent, and in May, 1952, the patient was given daily 25 mg. of methyltestosterone sublingually. Itching lessened in five days, and within two weeks had completely disappeared. The pruritus remains controlled by 25 mg. of methyltestosterone four times a week.

Case 7.—A 48-year-old woman suffering from post-operative stricture of the common hepatic duct was operated on in September, 1948, for the removal of a cyst of the cystic duct. In May, 1949, she first experienced attacks, lasting about a day, of sudden epigastric pain with rigors, fever, and jaundice. These recurred every two to three weeks. Pruritus developed which was maximal during the attacks but was also experienced during the intervening periods. The patient was again operated on in June, 1951. A stenosis of the common hepatic duct was discovered, and an attempt to reconstruct the duct was only partially successful. The attacks continued and were still associated with pruritus, which caused her the acutest distress. In June, 1952, she was started on daily sublingual methyltestosterone, 25 mg., and in four days the pruritus ceased. Although the attacks of jaundice, rigors, and fever continue, there has been no recurrence of pruritus.

Comment on Cases

The subjects treated and the results obtained are summarized in the Table. Some side-effects of testosterone were recorded.

Effect of Sublingual Methyltestosterone (25 mg. daily) on Pruritus in Obstructive Jaundice

Case No.	Sex and Age	Diagnosis	Duration of Pruritus	Time Taken for Relief	Serum Bilirubin mg./100 ml.		Serum Total Cholesterol mg./100 ml.	
					Initial	Rise*	Initial	Fall*
1	F 54	Primary biliary cirrhosis	14 mths	7 days	10·0	8·5	600	180
2	M 54	,, ,,	3 years	5 ,,	12·2	2·0	290	90
3	F 69	Hepatic duct carcinoma	3 mths	6 ,,	3·7	9·3	550	220
4	F 79	,, ,,	7 ,,	6 ,,	18·0	4·0	800	380
5	F 45	Stone in common bile duct	6 weeks	4 ,,	—	—	—	—
6	F 41	Primary biliary cirrhosis	18 mths	5 ,,	7·8	6·0	640	220
7	F 48	Stricture of bile duct	46 ,,	4 ,,	—	—	—	—

* Values six weeks after beginning of methyltestosterone therapy.

The *depth of jaundice* tended to increase. Patients with continuing unrelieved bile-duct obstruction would be expected to show a steady deepening of icterus. However, with one exception (Case 5), the patients studied had been jaundiced for so long a time that the rate of increase had become very slow. In all the five subjects in whom serial serum bilirubin values were available testosterone seemed to increase the rate of rise of serum bilirubin. Patients should be warned that the testosterone therapy may make them more yellow and that this does not indicate a worsening of their liver function.

The *serum total cholesterol* tended to diminish. This was particularly so when the pre-treatment values were very high. A patient with a normal initial value (Case 2) showed only a slight fall with testosterone therapy.

Masculinization was noticed in three patients. Case 1 developed hirsuties nine months after starting daily sublingual therapy. The voice deepened. This necessitated stopping the drug. Treatment was resumed with 25 mg. sublingually every other day. Pruritus remained controlled and the masculinization has not progressed. Case 6 noticed a few hairs appearing on the chin within 11 weeks of beginning sublingual testosterone, 25 mg. daily. Dosage was reduced to 25 mg. three times a week, and the hirsuties has not progressed; itching has not recurred. Case 4 also developed some hirsuties three months after starting sublingual therapy. This did not distress the patient, and the testosterone was continued. The three other female patients in this series did not receive testosterone long enough for endocrine complications to develop.

Discussion

Pruritus cannot be evaluated objectively, and the value of any drug used in its treatment is very difficult to assess. The failure of "dummy" inert tablets to relieve the pruritus in two of our patients and the use of a "neutral" observer to assess the results helped to circumvent this difficulty. Pruritus may disappear spontaneously during the course of obstructive jaundice, even though the bile-duct occlusion is not relieved. This is usually associated with failure of liver-cell function. This could hardly explain the relief from pruritus in all of the patients treated in this series, particularly as in three subjects the itching recurred when the testosterone was withdrawn.

Testosterone propionate has been successfully used in the treatment of senile pruritus (Feldman *et al.*, 1942). There are few reports of its use in jaundice. Ahrens and his group gave 25 mg. of methyltestosterone daily by mouth to three patients suffering from the itching of primary biliary cirrhosis: in two there was conspicuous relief; in the other the testosterone had little effect. Parkinson (1952) was successful with oral testosterone in treating pruritus in a patient suffering from biliary cirrhosis.

The seven cases reported above all made a dramatic response to oral testosterone. The rationale of this therapy is not known. Pruritus in jaundiced patients is often attributed, on rather slender evidence, to irritation of cutaneous sensory nerves by retention of bile salts in the blood. Blood-bile-salt levels, however, do not correlate with the incidence of pruritus (Snell and Keyes, 1933; Sherlock and Walshe, 1947), and attempts to initiate or aggravate pruritus by giving bile salts have usually failed (Brulé and Cottet, 1942; Sherlock and Walshe, 1947). Moreover, bile salts incorporated in a lotion have been successfully used in the treatment of pruritus due to primary skin disease (Brulé and Cottet, 1942). Flink and Williams (1952) relieved pruritus with corticotropin in five patients with obstructive jaundice, and related this to a small fall in the blood-bile-salt level. The subjective improvement could equally well be correlated with the feeling of well-being induced by corticotropin. Other steroids have had limited trials for antipruritic effect. Ahrens and his co-workers, using progesterone and oestradiol, failed to influence pruritus in four patients suffering from primary biliary cirrhosis, but further trials are needed with other steroid drugs.

A high serum cholesterol and serum lipid level develops in prolonged obstructive jaundice of whatever cause. The

extent of the elevation can be correlated with the occurrence of skin xanthomas (Ahrens *et al.*, 1950). Testosterone lowers the total serum cholesterol level in primary biliary cirrhosis (Ahrens *et al.*, 1950; Parkinson, 1952), and we have confirmed this finding. This further action of testosterone in obstructive jaundice may therefore prevent or ameliorate the xanthomatous skin lesions.

Absence of bile from the intestines leads to steatorrhoea with imperfect absorption of calcium and the fat-soluble vitamins. Patients with prolonged obstructive jaundice develop secondary changes in the bones with kyphosis, spontaneous fractures, and radicular pain. Androgen administrations result in a diminished urinary loss of calcium and phosphate and a conspicuous fall in urinary nitrogen (Reifenstein and Albright, 1947). Testosterone may therefore have an additional beneficial effect on the bone lesions of obstructive jaundice.

We have confirmed the rise in the serum bilirubin level in jaundiced patients given testosterone. Methyltestosterone has even been implicated as the cause of an obstructive type of jaundice in seven non-jaundiced patients receiving the drug for its androgenic action (Werner *et al.*, 1950). The mechanism of the jaundice is not known. The increase in the depth of jaundice should not be a contraindication to giving testosterone for its antipruritic action.

Masculinization in female patients is an unfortunate complication of testosterone therapy. Most patients are, however, willing to suffer this disability if the intolerable itching can be alleviated. The exact amount of testosterone needed to prevent itching is still unknown. In some subjects it may be possible to give just enough to relieve the pruritus and yet not induce masculinization. It is suggested that in female patients treatment should be started with 25 mg. of sublingual methyltestosterone daily for three weeks. This dose can then be given three times a week. In some patients it may be possible to reduce the dosage still further and still prevent itching. Male patients with chronic obstructive jaundice show signs of androgen deficiency, and benefit by the full daily dosage of 25 mg. of methyltestosterone sublingually.

Subcutaneous implants of testosterone propionate would seem to be an ideal method of exerting a continuous antipruritic effect. This is true if absorption is adequate (Case 2). However, in some patients absorption is very slow (Cases 1 and 4) and pruritus continues unrelieved. Subcutaneous testosterone propionate implants have therefore proved unreliable, and sublingual methyltestosterone administration is recommended for routine use.

Summary

Methyltestosterone (25 mg. daily sublingually) relieved pruritus within seven days in seven patients suffering from chronic obstructive jaundice. The rationale of this therapy is not known. Testosterone propionate by subcutaneous implant was not so effective, perhaps owing to inadequate absorption.

Other effects of prolonged testosterone therapy were an increase in the depth of jaundice, a fall in the serum cholesterol level, and masculinization in three of the six female patients treated.

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TETANUS SUCCESSFULLY TREATED WITH GALLAMINE TRIETHIODIDE

BY

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The treatment of tetanus falls into two parts—an attack on the infecting organism and control of the muscular spasms. The infecting organism is dealt with by giving toxoid and antitoxin in amounts and by routes which vary widely, but all authorities agree in advising heavy dosage, some recommending intrathecal injection in addition to the intravenous and intramuscular routes; wound toilet is performed.

In the past, control of spasms has been attempted by heavy sedation, and since the introduction of the muscle-relaxing group of drugs D-tubocurarine and mephenesin have both been used in the treatment of tetanus. In this country, Spencer Wells (1858–61) was the first to describe the treatment of tetanus with woorara, which contains an active principle, curarine, isolated by Boussangault in 1828; of three cases treated, one recovered. Only two years previously Claude Bernard (1856) had given his original description of curare and discussed its mode of action.

Difficulties in Treatment

During subsequent years the use of curare in the treatment of tetanus has been reported on many occasions, but Cole (1934) and other authors have noted the difficulties for long encountered owing to the lack of a standard preparation. Ory and Grossman (1948) reported two recoveries after the use of curare; they found that the drug caused too much relaxation, the tongue often falling back and causing respiratory obstruction. They also advised the use of atropine to counteract increased bronchial secretion, another troublesome feature in cases receiving curare. Adriani and Ochsner (1947), commenting on five cases treated with curare, stated that one patient died an hour after the administration of a single dose of curare which had been followed by respiratory and circulatory failure; the cause of death was not determined but was probably in part due to curare. They found that the action of curare was extremely abrupt in onset and that the effective response lasted for an average of 20 to 30 minutes. As the dose needed to relieve spasm was too close to that causing complete curarization, they had great difficulty in avoiding respiratory depression and obstruction.

Godman and Adriani (1949), reviewing the management of cases of tetanus, felt that true evaluation was difficult owing to the wide variations between individual cases. They thought that, while the control of rigidity and spasm was essential, no relaxant was entirely satisfactory. For mild cases they preferred a combination of phenobarbitone and "tolserol" (mephenesin), but admitted that though barbiturates were good as sedatives they were of little use as relaxants unless given in doses which would produce anaesthesia. Except in mild cases they recommended early tracheotomy in order to prevent downward spread of upper respiratory infection. Their experience with curare and with curare in oil was unsatisfactory.

Weed *et al.* (1948) used D-tubocurarine in wax and oil successfully in three cases. They found that a prolonged relaxant effect was produced without many of the unpleasant side-effects of curare, and that, while injections often did not need repeating until 18 to 24 hours had elapsed, the daily requirement of the drug increased progressively. Their findings were confirmed by Binger and Devnich (1950), who treated two cases with a similar preparation. Their aim was to produce relaxation without causing apnoea ; they reserved sedatives and hypnotics for use at night.

Trial of Gallamine

It will be seen that success has been hampered by the difficulty of maintaining the degree of relaxation required on a steady level owing to the comparatively short period over which all these drugs, with the exception of curare in wax and oil, produce sufficient effect. There is also the difficulty of giving adequate dosage without embarrassing respiration. Doughty and Wylie (1951) and Thompson and Norton (1951) report that respiratory depression is less marked with gallamine triethiodide than with D-tubocurarine, especially in the conscious subject. For this reason it was decided to try the effect of administering gallamine ("flaxedil") for the control of tetanic spasms.

Case Report

A married woman, a typist aged 35, was admitted to hospital at 1 a.m. on May 12. Four days previously she had first noticed difficulty in swallowing, trismus, and breathlessness on exertion. These symptoms continued, and on the day before admission stiffness of the muscles of the back of the neck and shoulders developed. At times she noticed a feeling of tightness in her abdominal muscles, but there was no definite history of spasms. For some months she had suffered from cracks in the finger-tips, and a fortnight previously a septic thumb had developed, which healed slowly. She had never been immunized against tetanus or received tetanus antitoxin.

Examination showed an alert and co-operative woman of average build. Her temperature was 99° F. (37.2° C.), pulse 100, and respirations 16. Mucous membranes were pale. Definite trismus and stiffness of the neck muscles were present. Two upper molars were carious. Hypertonus of the abdominal muscles was pronounced. On one thumb there was a small scar. No other abnormal physical signs were present.

Tetanus was diagnosed, and at 2 a.m. 100,000 units of tetanus antitoxin was administered intravenously. At 6 p.m. 200,000 units was given ; which dose was repeated daily until May 16, followed by 100,000 units daily until May 19. In addition, tetanus toxoid, 1 ml., was given on May 12. The patient was nursed in a single-bedded room and a special nurse was provided.

Trismus and dysphagia increased after admission, and on May 13 feeding was started by means of a Ryle's tube passed intranasally ; this was maintained until May 28. On May 13 her breathing was becoming laboured and bronchial secretions were expelled with difficulty. Her temperature rose to 101.4° F. (38.5° C.), and her pulse to 120. Scattered rhonchi were present on auscultation, so crystalline penicillin, 500,000 units eight-hourly, was begun. On May 15 she had well-marked risus sardonicus and was unable to protrude her tongue, as her front teeth could be separated only ¼ in. (0.6 cm.). Muscle hypertonus was pronounced and tetanic spasms were occurring with increasing frequency and severity.

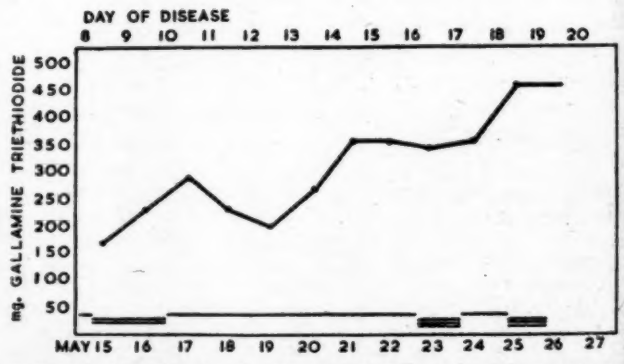
At this stage it was decided to try the effect of gallamine in reducing the severity of the spasms. An initial dose of 40 mg. was given intravenously ; within one minute there was relaxation of the abdominal muscles and diplopia. Diaphragmatic respiration became exaggerated, but for six minutes there was considerable weakness of the intercostal muscles. One hour later the patient was comfortable and able to open her mouth a little. Three hours after the injection trismus had returned and further frequent tetanic spasms were occurring.

The effect of gallamine intramuscularly was next tried: an injection of 80 mg. was followed by abolition of all but slight transitory spasms, swallowing became possible, but coughing remained difficult. Four hours later a further 40 mg. intramuscularly and ¼ gr. (16 mg.) of morphine sulphate subcutaneously allowed the patient to obtain several hours' light sleep. For the next 16 hours 30 mg. of gallamine was given four-hourly by intramuscular injection, but during the afternoon of May 16 the dose was increased to 40 mg. three-hourly, as spasms, although no longer painful, were still occurring.

On May 17 the patient's general condition was unchanged, but as the spasms were not completely controlled by intramuscular injections and as frequently repeated injections by this route were thought undesirable, a slow intravenous saline drip was begun, and gallamine was injected into the rubber tubing of the drip at a dose of 10 mg. each hour. Morphine sulphate, ¼ gr. (16 mg.), and amylobarbitone sodium, 3 gr. (0.2 g.), were given nightly. Next day she was cheerful and felt better after a moderately good night's sleep, no further muscle spasms having occurred since shortly after the drip was started. Pyrexia—99° F. (37.2° C.)—continued and was associated with a low-grade respiratory infection, crepitations being present, especially at the base of the left lung. The haemoglobin was 47% (6.9 g.%) and the white cells numbered 14,500 (polymorphs 84%, lymphocytes 14%). Penicillin was discontinued, and sulphamerazine, 1 g. eight-hourly, was given in the form of "cremomerazine" through the Ryle's tube.

On May 19, as no further spasms had occurred, the frequency of gallamine injections into the drip was reduced to 10 mg. every 90 minutes ; but next day, as slight spasms had occurred during the night, the dose was increased to 10 mg. hourly, being further increased to 15 mg. hourly in the evening.

On May 21 the patient's general condition remained unchanged. Her temperature was 99° F. (37.2° C.). She was free from spasms, except for one short period when the drip became blocked. As the anaemia was not responding to colloidal iron by the Ryle's tube, a transfusion of 1 pint (570 ml.) of blood was given on May 22 and repeated on May 24. Sulphamerazine was discontinued, and gallamine was continued at the rate of 15 mg. hourly until the afternoon of May 23, when, in view of the depletion of available veins, it was decided to change to a subcutaneous infusion, to which was added hyaluronidase, 1,000 units, six-hourly. It required 14 mg. of gallamine hourly by this route to keep the patient free of spasms. While the second blood transfusion was being given the gallamine was again administered intravenously. Slight facial spasms occurred on May 25, so the dose was increased to 20 mg. hourly.



Daily requirement of gallamine triethiodide and route by which administered. (Intravenous, —— ; intramuscular, = ; subcutaneous, ≡ .)

By the morning of May 26 the patient was able to open her mouth a little wider. At 11 p.m. she was found to be perspiring freely, the respiration was gasping in character, and her muscles were extremely relaxed, so the drip was stopped, and by 1 a.m. she was quite comfortable. The next morning she was breathing without difficulty and no sign of muscle spasm remained : she was alert after a very restful night. No further gallamine was required. On May 28 she was able to eat solid food. Although muscle tone remained increased, no further spasms occurred. Respiratory infection resolved rapidly, the low-grade pyrexia ended on May 30, and her general condition steadily improved. The anaemia did not respond to oral iron, and an iron-absorption test showed no absorption. A course of "ferrivenin" totalling 1.47 g. was given, raising the haemoglobin to 82% (12.1 g.).

Over the 11½ days of continuous administration 3,710 mg. of gallamine triethiodide was administered (see Chart). At no time was an oxygen tent or artificial respirator required.

Summary

A case of tetanus is described which began about two weeks after a minor injury to a thumb that had become septic. At the time of admission trismus and hypertonus were present. By the eighth day of the disease it was obvious that the increased frequency and severity of the tetanic spasms would not respond to normal sedation with barbiturates and morphine, and it was decided to try the effect of gallamine. At first this was administered intramuscularly, but three-hourly injections proved insufficient to control spasms. Hourly injections into the rubber tubing of a saline intravenous drip were found to be satisfactory, as was administration hourly into a subcutaneous hyaluronidase infusion.

As the days passed it became noticeable that steadily increasing amounts of gallamine were required to prevent spasms ; in view of this, the sudden termination of the tetanic spasms was quite unexpected. Morphine sulphate, ¼ gr. (16 mg.), and amylobarbitone sodium, 3 gr. (0.2 g.), were administered each evening and at other times as required.

We wish to thank Drs. Sheila Watts and Pamela J. Houchin for their continuous and untiring help in the supervision and treatment of this patient. We gratefully acknowledge the information provided by the Medical Information Division of Pharmaceutical Specialities (May & Baker) Ltd. and used in the preparation of this paper.

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At the anniversary meeting of the Royal Society on December 1 Dr. E. D. Adrian, in his presidential address, paid a special tribute to Sir Charles Sherrington, who died last March at the age of 94. He had been president of the Royal Society from 1920 to 1925. In Dr. Adrian's words, "few scientists of our time have been so well qualified to judge the advance of human understanding of the natural world, for he lived long enough to have witnessed most of the great achievements of the present era, and he had made an intimate study of the science of the Middle Ages, when the schoolmen and alchemists were as satisfied with their theories as we are with ours."

PROLONGED WOUND ANALGESIA AFTER SURGICAL OPERATIONS

CLINICAL TRIAL OF EFOCAINE

BY

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Post-operative pain is an almost universal sequel to every type of surgical procedure and, apart from causing distress to the individual patient, contributes to a number of secondary complications such as inhibition of the cough reflex and consequent pulmonary collapse, retention of urine, delayed mobilization leading to venous stasis and thrombosis, loss of sleep, and delayed convalescence.

The aqueous solutions of local analgesics hitherto in use have suffered from the disadvantage of rapid diffusion and elimination from the area of infiltration, so that even with the addition of adrenaline the effect is unlikely to last for more than four hours. Oily solutions such as "proctocaine" and benzocaine compound injection *N.F.* (A.B.A.) have been inconsistent in their action, and have caused trouble from abscess formation and local necrosis.

American workers (Iason and Shaftel, 1952a, 1952b ; Puderbach and Shaftel, 1952 ; Raicus, 1952 ; Weinberg, 1952) have recently described a new product marketed under the name of "efocaine," composed of procaine base 1%, with procaine hydrochloride 0.25%, and butyl *p*-aminobenzoate 5% in propylene glycol 78% and polyethylene glycol 300 2%. This clear solution is non-oily, though somewhat viscous, and is freely miscible with body fluids ; none of the constituents appear to have any toxic effects. The solution is saturated, but on contact with the body fluids the local analgesic is immediately precipitated in a relatively insoluble form which exerts an effect for from 8 to 20 days.

Clinical Trial

In order to obtain experience of the use of this product and to assess its therapeutic possibilities, a series of patients were selected who were undergoing the commoner operations in which post-operative pain usually necessitates the administration of analgesic drugs. The first two cases were elective appendicectomies performed through McBurney incisions. At the conclusion of the operation, before peritoneal closure, the solution was introduced into the intermuscular plane above and lateral to the incision, 5–6 ml. being used. The wounds were insensitive for the whole of the patient's stay in hospital (eight days), but both patients complained of intestinal discomfort for the usual 36 hours.

Having established that prolonged analgesia of a small wound could be obtained, a regional block of T 11 and 12 and L 1 (2 ml. each nerve) was then attempted in a nephroureterectomy for renal tuberculosis, with a right paramedian as well as a lumbar incision. Here there was a good deal of pelvic dissection, which resulted in abdominal discomfort. Complete analgesia was not achieved, but the lumbar incision remained partly anaesthetic for 20 days. A similar lumbar block of T. 11 and 12 and L. 1 was performed on a patient after left lumbar ganglionectomy by the anterolateral route. There was no post-operative pain and the scar was only slightly sensitive on the twelfth day.

Three inguinal hernia patients were given 10–12 ml. of the solution, partly into the intermuscular plane near the iliac

Case	Sex and Age	Operation	Method of Administration	Effects	Comment
1	F 25	Interim appendicectomy	6 ml. infiltrated into intermuscular plane lateral to wound	Intestinal discomfort 36 hours. Anaesthesia of wound for 7 days +	Good
2	F 12	Appendicectomy and removal of fimbrial cyst	5 ml. infiltrated (as above)	Abdominal discomfort 24 hours. Anaesthesia of wound for 8 days +	..
3	F 23	Nephro-ureterectomy for renal tuberculosis	Regional block T. 11, 12, L. 1 (2 ml. each nerve)	Partial analgesia of wound for 20 days. Abdominal discomfort 3–4 days	Fair
4	M 55	Perforated duodenal ulcer	7 ml. into rectus sheath and subcutaneous tissue on each side	No apparent effect	Failed
5	M 35	Haemorrhoidectomy (St. Mark's)	10 ml. round inferior haemorrhoidal nerve and into sphincters	Painless convalescence. Anal anaesthesia for 10 days and slight retention of urine	Good
6	M 57	Vagotomy and gastroenterostomy	10 ml. into right intercostal block, T. 7–11, also into left rectus sheath	Slight wound discomfort on coughing. Sensation back to normal in 6 days	Fair
7	M 60	Vagotomy and gastroenterostomy	20 ml. given as bilateral intercostal block T. 7–11	No post-operative pain. Slight discomfort on coughing. Wound insensitive 10 days +	Good
8	M 62	Abdominal vagotomy	20 ml. given as bilateral intercostal block T. 7–11	No post-operative pain. Wound anaesthesia 7 days +	..
9	M 68	Left antero-lateral lumbar ganglionectomy	6 ml. regional block T. 11, 12, L. 1 (2 ml. each nerve)	No post-operative pain. Scar remained slightly sensitive	Fair
10	F 55	Right inguinal hernia	Local intermuscular and subcutaneous infiltration	No apparent effect	Failed (obese patient)
11	M 40	.. .. ..	12 ml. by local infiltration and round L. 1 near iliac spine	Slight wound haematoma. No definite anaesthesia	Failed
12	M 42	Partial gastrectomy	18 ml. bilateral intercostal block T. 7–12	No post-operative wound pain even on coughing. Skin anaesthesia not definite	Good
13	M 47	Haemorrhoidectomy (St. Mark's)	10 ml. round inferior haemorrhoidal nerve and sphincters	No post-operative pain (5 days)	..
14	M 42	Left inguinal hernia	10 ml. infiltrated in intermuscular plane round ilio-hypogastric nerve and subcutaneously	Complete analgesia 5 days +. Haematoma	..

spine so as to block the ilio-hypogastric and ilio-inguinal nerves, and partly subcutaneously to desensitize the skin incision. The first case was an obese woman with a direct hernia, and was unsuccessful, presumably owing to difficulty in accurate placing of the analgesic and its dissipation in the subcutaneous fat. In the second there was little post-operative pain, though actual skin anaesthesia was not achieved; in the third there was complete abolition of both post-operative pain and wound sensitiveness.

Two patients subjected to haemorrhoidectomy by the St. Mark's technique received, at the conclusion of the operation, 10 ml. of efocaine, 2.5 ml. being injected round each inferior haemorrhoidal nerve and about 5 ml. round the subcutaneous sphincter. Complete abolition of pain was achieved and neither patient required post-operative sedation. The first patient, nevertheless, had slight difficulty in micturition for 24 hours, and later commented that he had difficulty in knowing whether he was defaecating or not, owing to the loss of anal sensation, which persisted for at least 10 days. The second patient is analgesic at the time of writing (five days).

Five patients subjected to upper abdominal incisions for gastric surgery were also treated. The first, a chronic bronchitic with perforation of a duodenal ulcer, received at the conclusion of the operation a total of 7 ml. of efocaine, injected into the rectus sheath and subcutaneously on each side of the wound. There was no definite effect. When more ample supplies of efocaine became available the four other patients were treated by anterior intercostal block: from 1–2 ml. was used in each space, and the seventh to the eleventh nerves were injected. One patient experienced slight discomfort on coughing and sneezing, and sensation had returned to normal in six days; he had received only 10 ml. of efocaine by right-sided intercostal block (T. 7–11) and infiltration of the left rectus sheath. In the remaining three patients rectus sheath infiltration was discarded, 18–20 ml. of efocaine being used exclusively for a bilateral intercostal block. Their wounds were painless for at least seven days, though the loss of actual sensation was patchy. In particular, one man, seen five hours after partial gastrectomy, was sitting up cheerfully in bed maintaining that he had no pain at all; his wound could be handled vigorously without causing discomfort, and he coughed strongly without distress: this did not, however, prevent him from developing post-operative bronchitis.

Difficulties

The relative viscosity of the solution to be injected necessitates the use of a locking syringe if a narrow-gauge needle is to be used, as otherwise the force required to inject the solution is likely to detach the needle and waste the solution. Wide-bore needles have a tendency to cause haematomata (two instances), though these have given no serious trouble.

The low diffusibility of the solution means that to be effective it must be deposited in close proximity to the nerve to be blocked. Wide infiltration of the wound area itself is unreliable, particularly in obese patients, owing to dissipation of the analgesic. The results have been far more consistent when accurate nerve-blocking was possible—for example, antero-lateral intercostal, or inferior haemorrhoidal. In some cases the impression was that the analgesia did not become maximal until after 48 hours.

Desensitization of a wound does not abolish pain due to visceral distension.

According to the American literature the injection of efocaine produces a burning pain, especially if too near the skin. All our patients have received injection while under general anaesthesia, and we have therefore no comment to make on this point.

Summary and Conclusion

The claim that efocaine can produce prolonged analgesia of an operation wound has been substantiated. Of 14 patients, a good result was obtained in 8, a fair result in 3, and there was no apparent effect in 3.

To be effective an adequate concentration must be deposited in close proximity to the nerves supplying the area: an accurate nerve block is therefore more efficient than local infiltration of the area.

By its means, analgesia of a wound for periods of from 8 to 20 days can be achieved.

The viscous solution should be used with a locking syringe and the needle kept moving to avoid depot formation. A wide-bore needle may lead to wound haematoma.

No undesirable effects have been observed; on the contrary, the atmosphere in a ward with several recent

operation cases was unusually cheerful and the need for post-operative drugs was much reduced.

The method would appear to be of value in controlling pain following operations on the chest, upper abdomen, loin, and ano-rectal region: it may also prove of value in the treatment of fractured ribs. It would appear to be less effective when obesity makes accurate placing of the solution difficult, and is contra-indicated in the presence of infection.

On theoretical grounds one would expect a reduction in secondary complications due to inhibition of the cough reflex and retention of urine, but our series is too small for the forming of any conclusions on this point.

I am indebted to my colleague Dr. James Rochford and to Messrs. Crookes Laboratories for supplies of efocaine and for helpful advice on the methods of use.

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COLLAGEN/CHONDROITIN SULPHATE RATIO OF HUMAN ARTICULAR CARTILAGE RELATED TO FUNCTION

BY

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In a study of the physical and biochemical changes which accompany the ageing of hyaline articular cartilage a preliminary examination of the two main components, collagen and chondroitin sulphate, showed a very different ratio in some joints compared with others. This is, I suggest, related to mechanical function, since weight-bearing and non-weight-bearing areas of articular cartilage differ significantly in collagen and chondroitin sulphate content, whether comparison is made between joints or between different areas within the same joint.

Material and Methods

The material was taken within one hour of necropsy from adult patients whose articular cartilage showed no macroscopic evidence of senile change. Slices about 1 mm. thick were removed from the whole of the articular surface of the head of the humerus and the lower end of the homolateral femur: an aliquot was taken for analysis.

For comparison of weight-bearing and non-weight-bearing areas within an individual knee-joint, slices were taken from the following sites: (*a*) patellar surface of the femur, (*b*) the middle (weight-bearing) thirds of both femoral condyles, and (*c*) the posterior (non-weight-bearing) thirds of both condyles. These samples were compared with cartilage from (*d*) the centre of the medial surface (non-weight-bearing) of the humeral head, and from (*e*) the superior (weight-bearing) surface of the head of the femur.

The cartilage slices were dried in acetone and then over sulphuric acid to constant weight. Determination of the hydroxyproline content was made according to the method of Neuman and Logan (1950a), and collagen values were obtained by multiplying the hydroxyproline figures by 7.5 (Neuman and Logan, 1950b).

Chondroitin sulphate was determined by estimation of hexosamine after hydrolysis according to the method of Elson and Morgan (1933). The factor for conversion of hexosamine to chondroitin sulphate is approximately 4 (Einbinder and Schubert, 1950).

Results

Table I gives the results of five typical estimations. It is evident that the chondroitin sulphate content of knee cartilage is greater than that of the shoulder, but that the reverse holds for collagen.

TABLE I.—*Collagen and Chondroitin Sulphate Content of Healthy Articular Cartilage: Comparison of Knee and Shoulder (% of Dry Weight)*

Case	Age	Collagen		Chondroitin Sulphate		Collagen/ Chondroitin Sulphate Ratio	
		Knee	Shoulder	Knee	Shoulder	Knee	Shoulder
1	38	66·0	75·0	22·4	14·4	2·9	5·2
2	49	52·5	69·8	20·8	16·4	2·5	4·3
3	55	63·0	74·3	22·8	17·2	2·8	4·3
4	60	59·3	67·5	19·6	14·8	3·0	4·6
5	66	51·0	69·8	22·0	15·6	2·3	4·5

Table II shows that if comparison be made between joints (or between different areas within the same joint) the content of chondroitin sulphate is greater and the collagen less in weight-bearing articular cartilage than in cartilage which bears no weight.

TABLE II.—*Collagen and Chondroitin Sulphate Content of Weight-bearing and Non-weight-bearing Articular Cartilage (% of Dry Weight) in Man Aged 55*

Joint	Site	Collagen	Chondroitin Sulphate	Collagen/ Chondroitin Sulphate Ratio
Weight-bearing: Knee (articular surface of femur)	Medial condyle (middle third)	47·3	24·8	1·9
	Lateral condyle (middle third)	50·3	24·0	2·1
	Patellar surface	49·5	23·6	2·1
Hip ..	Head of femur	50·3	23·6	2·1
Non-weight bearing: Knee (articular surface of femur)	Medial condyle (posterior third)	57·8	18·8	3·1
	Lateral condyle (posterior third)	59·3	16·0	3·7
Shoulder ..	Head of humerus	66·0	16·8	3·9

Although, strictly speaking, the patellar articular surface of the femur is not weight-bearing, it is an area subject to marked shearing action, and its composition resembles that of weight-bearing cartilage.

Discussion

The importance of mechanical function in determining the composition of articular cartilage is illustrated by the results shown above: the greater resilience needed in weight-bearing areas is provided by a higher polysaccharide content.

It is well known that the earliest degenerative changes in the knee occur on the middle third of the articular surface of the medial femoral condyle and on the femoral patellar surface. It is conceivable that the susceptibility to degeneration of weight-bearing or stressed sites is related to the special structural adaptation to function revealed by the above analysis. It is hoped in future work to test this hypothesis.

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Medical Memoranda

Occupational Trophic Ulcer in Tabes Dorsalis

Trophic changes involving the skin of tabetics are usually confined to perforating ulcers of the foot, first described by Duplay and Morat in 1873, and to intractable sacral and lumbar ulceration in those patients who are confined to bed. Both types of case are the result of trauma to an area where there has been a definite reduction in the perception of deep pain and often light touch, in addition to a probable reduction in vascular supply due to specific arteritis or periarteritis.

The following case of extensive trophic ulceration occurring over the greater trochanter in a case of tabes dorsalis is rare enough to be of interest. An extensive search of the literature has revealed no similar case.

CASE REPORT

A man aged 53 was admitted to hospital on June 13, 1950, with a history of repeated "fainting attacks" during the previous four months. He had returned to consciousness by the time he was admitted. Physical examination revealed no abnormality in the cardiac or respiratory systems. Neurological examination showed: bilateral ptosis and slight wrinkling of the forehead; bilateral Argyll Robertson pupils; biceps- and supinator-jerks present and equal; triceps, knee-, and ankle-jerks absent; plantar responses not elicited; Romberg's sign present; vibration sense absent. There was a diminution of sensation to touch and pin-prick, generalized over the lower limbs, with complete anaesthesia over the soles of the feet, genital region, and perineum. The blood Wassermann reaction was positive 1:16 and the Kahn test was positive. Examination of the cerebrospinal fluid showed: cells, 70 per c.mm.; protein, 80 mg. per 100 ml.; globulin, increased; Wassermann reaction positive 1 in 3; Lange 4555432100.

After five weeks' antisyphilitic treatment in hospital the patient was discharged to attend the special treatment centre. He attended on three occasions only and then defaulted from treatment on August 15. Four months later he reattended because he thought he had "a boil or something on his leg which had been there for a month and was getting bigger."

On examination a large painless ulcer was seen, measuring approximately 4 in. (10 cm.) across, involving the skin and subcutaneous tissues over the greater trochanter of his left femur. The muscles and greater trochanter were clearly visible in the floor of the ulcer and the edge was clean-cut. No signs of granulation were present, but there was some purulent discharge from the depths of the ulcer (see illustration). An *x*-ray film revealed no underlying bone disease.

Trophic ulceration of the buttock in tabes dorsalis. The greater trochanter is visible.

Physical examination revealed the same signs as before, except that a more thorough sensory examination showed almost complete anaesthesia over both buttocks, thighs, and the perineum.

He was readmitted to hospital, and, on investigating his history to elucidate the reason for this unusual site for what was apparently a trophic ulcer, it was found that he was a firewood seller and did his rounds with a pony and cart. His usual seat was on the buckboard in front, or on the offside shaft, and he invariably sat on his left buttock and thigh, with his right leg crossed over the left knee. It is thought that the constant trauma and increased pressure over the greater trochanter, brought about by sitting in this position and constantly mounting and dismounting from the cart, were enough to produce a trophic ulcer. This was particularly likely to occur as he was rather thin and the area involved was anaesthetic.

COMMENT

There would seem to be little doubt that the ulceration occurring in this case can be termed trophic, and that the unusual site is accounted for by the man's occupation. It is important to consider other possible causes of ulceration in a syphilitic patient. Gummata occur in places that are liable to trauma, but they all show signs of healing under antisyphilitic treatment. Indeed, many of them will heal on potassium iodide therapy alone. In this case there was no sign of healing in spite of the administration of a variety of antisyphilitic drugs over many weeks.

Another possibility is a bismuth track abscess, but the only injections of bismuth given to this patient were of a rapidly absorbable oil-soluble bismuth, and the last injection had been given at least four months before the appearance of the ulcer. Gangrenous ulceration complicating diabetes is far commoner at the lower end of the extremity, and this patient had a normal blood sugar.

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Influenza Epidemic in Ankara

A moderate epidemic of influenza broke out in Ankara in the first week of December, 1950, and there were also short outbreaks in other Turkish cities. The clinical features were typical though not severe. In many cases the temperature rose to 39–40° C. (103.4–104° F.), and slight bradycardia was often present. Most patients had only slight symptoms, such as coryza and tracheitis. A large proportion of the patients were children. The central nervous system was not attacked, and there was no unusual incidence of pneumonia. A-type antibodies were found in specimens of sera obtained from many patients.

Influenza is not a notifiable disease, and we have no exact figures of morbidity rates. During the epidemic the morbidity rate at three elementary schools visited (about 1,850 pupils) was about 40%. During the peak of the epidemic 18% of the pupils were absent on one day. Morbidity rates elsewhere in Turkey ranged between 10% and 30%.

The viruses were tested with the standard sera of A and B types (by courtesy of Dr. C. H. Andrewes) and typed as A. Dr. Andrewes and Dr. A. Isaacs reported in a personal communication that the viruses were type A-prime. During a second wave of the epidemic three strains isolated by Dr. Berke were also found to be type A-prime. Dr. Andrewes has informed me that all the strains sent to the World Influenza Centre in London were A-prime. The same type of virus also caused the epidemic in England (Potter, 1951). These findings suggest that air transport is playing an important part in the spread of influenza throughout Europe.

I am indebted to Dr. C. H. Andrewes and Dr. A. Isaacs for typing the viruses.

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Reviews

NEW TEXTBOOK OF MEDICINE

The Principles and Practice of Medicine: A Textbook for Students and Doctors. By L. S. P. Davidson, M.D., F.R.C.P.Ed., F.R.C.P.Lond., M.D.Oslo, and the Staff of the Department of Medicine and associated Clinical Units. (Pp. 919; 57 figures. £1 12s. 6d.) Edinburgh and London: E. and S. Livingstone. 1952.

This Edinburgh textbook presents many of the advantages of single authorship with none of its disadvantages. It comes from the staff of a single department of medicine, and the 14 authors have worked under the editorship of the head of the department, Professor L. S. P. Davidson. Moreover, it has been founded on the notes of the lectures in medicine which are given every year, and is therefore the product of a good deal of unified experience.

The author of a student's textbook of medicine to-day is faced with two problems. The first is what to leave out. He may, of course, leave out nothing, like the majority of American editors, whose textbooks have grown more and more Gargantuan in recent years, so that a special assignment method of teaching has had to be devised to cope with them. Professor Davidson has omitted accounts of the acute systemic infections and the psychiatric disorders. It is certainly a surprise to look up the index of a textbook of medicine and to find no reference to undulant fever and hysteria, although nutritional disorders and tropical diseases are included. The second problem is how to deal with what is left, and, in particular, how to handle the rarities. Some of the sections in this textbook approximate to an essay rather than a synopsis, and this seems to be the right method. All the sections include an account of the anatomy and physiology of the particular system, and methods of prevention of disease. Some of the rarities are mentioned by title only, and here there might have been a case for an occasional reference to the literature. The several sections are lucidly written, and a balanced account is given of the diseases with which the student may be expected to become familiar during his course of study. The format is similar to the *Textbook of Medical Treatment* by Davidson, Dunlop, and McNee, to which this may be regarded as a companion volume. It is a pleasant book to read and sits comfortably in the lap. It is up to date, though just not in time to note the haemotoxic effects of chloramphenicol. It sells at a reasonable price, and can be strongly recommended as a textbook of medicine for students working for their final examination.

L. J. WITTS.

LUNG TUMOURS

The Diagnosis and Treatment of Intrathoracic New Growths. By Maurice Davidson, D.M., B.Ch.Oxon., F.R.C.P. With a chapter on Radiotherapy by David W. Smithers, M.D.Cantab., M.R.C.P., D.M.R., and a chapter on Operative Treatment by Oswald S. Tubbs, M.B., B.Chir., F.R.C.S. Oxford Medical Publications. (Pp. 260; 170 figures. £2 2s.) London: Geoffrey Cumberlege (Oxford Medical Publications). 1951.

This monograph is chiefly concerned with the aetiology, incidence, diagnosis, and treatment of tumours which grow in the bronchial tree and the lung. To this have been added observations on some lesions which affect the mediastinum. The title is more comprehensive than the contents, for only passing reference is made to tumours of the oesophagus, the heart and the pericardium, the diaphragm, the ribs and intercostal muscles, the thymus, etc.

The main section of the work is from the pen of Dr. Maurice Davidson, whose clear style of writing and deep knowledge of the subject combine to produce a valuable and compact treatise, full of information and leavened with his own particular wisdom.

The place of radiotherapy in the management of these tumours is clearly set out by Professor D. W. Smithers. His contribution can be understood and appreciated even by those of us who are no longer quite sure what radiotherapy is. The impression that remains with your reviewer after reading this section is that radiotherapy will not cure these patients but that it may, and often does, alleviate some of the most distressing symptoms.

Mr. O. S. Tubbs writes about the surgical treatment. He does not attempt to cover all the details of the various surgical operations, but rather to give a general picture of the type of procedure necessary to remove these tumours. He discusses the implications of surgical treatment and weighs up the relative positions of radical surgery and conservative treatment.

The book contains no new information; it is a well-written review of current knowledge, and will be valuable not only to postgraduates studying for higher examinations but to many practitioners.

"The position, then, is that in this country some 9,000 persons develop bronchial carcinoma annually, of which perhaps no more than 2% have a pneumonectomy or lobectomy which are generally regarded as the only hope of cure. Little more than 10% have other forms of treatment which hold out any prospect of producing temporary arrest of tumour growth; and in only 4% is treatment, other than surgical, given which is even planned to attempt more than this. This means that at the moment attempts to cure these patients are only being made in about six cases in every 100."

It is hoped that the book may ameliorate this sad state of affairs.

N. R. BARRETT.

HOSPITAL PLANNING

Background to Hospital Planning. By Professor H. W. C. Vines, M.D., with foreword by the Rt. Hon. Lord Inman, P.C., J.P. (Pp. 188. £1 10s.) London: Faber and Faber. 1952.

In this book Professor Vines produces some of the fruits of his labour as chairman of the planning committee for the new Charing Cross Hospital, and the fruits are good. Indeed, the book is worth careful study not only by all engaged in planning a new hospital, but also by all busy with the more humdrum but much commoner task of adapting and re-equipping existing hospitals to make them reasonably efficient.

In the early pages Professor Vines points out—and how truly—that in very many British hospitals structure and equipment are sadly inferior and that, "if the Health Service is not to become the laughing-stock of continents, extensive building and reconstruction of our hospitals must be faced." He emphasizes that intensive study of the special problem of hospital planning is sorely needed, and he gives an enlightening picture of many fundamental requirements of patient care on which planning of hospital structure and equipment for general hospitals must be based.

His book is deceptively easy to read; it is short, the print is large and clear, and the reader can go straight through it with great pleasure and considerable profit, but several re-readings and much hard thinking are necessary for maximum profit. It is not a textbook in any sense of the word. Though full of useful information about hospital planning, the book's main virtues are that it goes to the root of some problems and that it stimulates thought and willingness to try new methods of hospital planning. To take only one example: it is common knowledge that in many large general hospitals patients are outnumbered several times by staff, but Professor Vines's suggestion may be new to many—that in the interests of the outnumbered patients in general hospitals of over 400 beds their cooking should be taken right out of the main kitchen, which should do the mass cookery required for feeding all types of hospital staff.

Altogether the book is intensely interesting and contains much of great value for hospital planners, doctors, nurses,

and committee members, and perhaps, above all, hospital architects. It whets anticipation of the day when the completed new Charing Cross Hospital may demonstrate some of the modifications of traditional planning advocated by Professor Vines.

W. G. PATTERSON.

THE ADAPTATION SYNDROME

The Story of the Adaptation Syndrome (told in the form of informal, illustrated lectures). By Professor Hans Selye, M.D., Ph.D.(Prague), D.Sc.(McGill), F.R.S.Canada. (Pp. 225. $4.50.) Montreal, Canada: Acta, Inc. 1952.

This book represents the slightly edited wire recordings of seven lectures given by Professor Selye. He discusses in an informal and fluent style the evolution of the stress concept, the adaptation syndrome, the role of the adrenal cortex and anterior pituitary gland in the adaptation syndrome, the diseases of adaptation, the part played by conditioning circumstances in modifying the results of stress, the "endocrine kidney," the effects of overdosage with adrenal cortical extracts, the interactions between the various hormones, the therapeutic value of hormones, and other subjects. The material used is limited almost entirely to observations made by Selye and his co-workers, and, as stated in the introduction, the book makes no pretence at either objectivity or completeness. The researches of the Montreal group are described in chronological order, and the evolution and growth of their ideas are put easily and succinctly before the reader.

Since the style is so persuasive it would perhaps be unwise to recommend this book to junior students, who may be unaware that some of the topics which are treated rather dogmatically are still open to discussion. For example, the "diseases of adaptation" are treated with the same degree of assurance as the description of the adaptive reactions to stress. Although many authorities would agree that varied types of stress evoke similar patterns of response on the part of the body, few would agree whole-heartedly with Selye's views on the aetiology of the "diseases of adaptation" in man. The author's views on research methods and research in general are freely interspersed in the text, and the straightforward common sense of these views may be recommended for the encouragement of those beginning research. This book will be of use to anyone who wishes to get generally acquainted with Selye's work and views but has not the time to consult his larger and more detailed publications.

G. W. HARRIS.

POLLUTED AIR

Atmospheric Pollution: Its Origins and Prevention. By A. R. Meetham, D.Sc. (Pp. 268; 81 figures. £1 15s.) London: Pergamon Press. 1952.

It is fitting that, at a time when the smoke abatement movement is rapidly gaining momentum and smokeless zones are springing up in crowded areas, an authoritative textbook on atmospheric pollution by such an acknowledged expert as Dr. Meetham should appear. This book is divided into 15 chapters dealing with such subjects as fuels, fuel-burning appliances, domestic requirements, industrial processes, then with atmospheric pollution, and finally with remedial measures and with the British and American law on the subject. At the end of each chapter there is a bibliography by means of which fuller information may be obtained on the subjects discussed in the chapter. There is also an index, which we have tested and have not found wanting. Dr. Meetham fully acknowledges his indebtedness to the Department of Scientific and Industrial Research and to the Fuel Research Station for permission to make available here so much Government-published material.

The account of the Teddington experiments on the speed of, and the circumstances which govern, the corrosion of metals is particularly interesting. It seems that there is a very great increase in the rate of rusting if the relative humidity is over 80%, and that rusting is most rapid when high humidity, sulphur dioxide, and particles are all present together. An important practical point is that chromium plate will not deteriorate if frequently washed.

On page 216 it is stated that over 500 persons die each year in the United Kingdom of cancer of the respiratory system. We wish this figure were an up-to-date truth, but it is not, and we feel it is sufficiently important for an erratum slip to be inserted. The latest figures available are to be found in the Registrar-General's Annual Report for 1949 as follows—lungs and pleura: males, 9,327; females, 1,945; total, 11,272. The figure of 500 is the approximate figure for 1921. But this was the only error we came across, and we heartily commend this book to all grades of public health staffs, architects, engineers, meteorologists, and members of local authorities, as well as to members of Parliament and to those of the intelligent general public who are acting as missionaries in the cause of the elimination of atmospheric pollution.

F. E. TYLECOTE.

AN APPLE A DAY

Fitness for the Average Man. By Sir Adolphe Abrahams, O.B.E., M.D., F.R.C.P. (Pp. 170. 10s. 6d.) London: Christopher Johnson. 1952.

It would not be surprising to find all the 170 pages of this intriguing little book devoted to an attempt to define its title, for both fitness and the average man would seem to be rather vague and widely encompassing conceptions. But the essentially practical and always pungent prose of the author sweeps aside the idea of such a waste of time, words, and paper. He proceeds after the briefest introduction of his stated theme to produce a series of vignettes which make equally good reading to either the medical man or the layman. None could be better qualified than Sir Adolphe to discuss the problems that link the various branches of medicine to those of exercise in general and sport in particular. Himself no mean athlete, he has made this field a lifelong study, and the results—expressed in concise and perfect English, interlarded with cogent simile and a faint streak of rather sardonic humour—are both interesting and stimulating. They show very clearly that this link between medicine and sport is in urgent need of much firmer forging. The fact that Sir Adolphe is the first president of a newly formed association to achieve this aim presages well for its future.

When one considers what a large proportion of the population of this country take part in various sports and recreational exercises, their problems and the reaction of our profession to them surely demand as intensive study as that now given, for instance, to industry and the Services. Such a conception lies behind most of the practical short articles of which this book consists. A list of the chapter headings on the cover would be well worth while. Who would not rise to the bait of "Too Old at Forty," "Doping," "Women and Athletics," "The Making of a Champion," "Brain and Brawn"?—to mention but a few. In one chapter the author deals with a series of old pseudo-medical quotations used every day in our everyday life—"Ne'er cast a clout till May is out"; "An apple a day keeps the doctor away"; "Hunger is the best sauce"; "A man is as old as his arteries," and so on. Each and all are discussed in a practical, succinct, and impartial manner. Each note contains the original thought of an original thinker.

It is not easy to write an essentially medical book for the lay public which will still interest the profession. This does. The author's definition of fitness as "the provision of antidotes to the consequences of modern existence" is as good a summary of the whole book as one could devise. Any doctor or layman who reads it will not only be interested and amused but also learn something of good common-sense value that he did not know before.

ARTHUR PORRITT.

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SMOKING AND LUNG CANCER

Six years ago the Medical Research Council called a conference to consider whether the remarkable increase in death rates from lung cancer, as indicated by the Registrar-General's statistics, justified a search for the causes of this phenomenon. At that time many were sceptical about the reality of the apparent rise, attributing it to the increasing use of radiography in the diagnosis of thoracic disease; but fortunately the conference was not deterred by such doubts from advising researches both of a statistical and an experimental nature. Among the conclusions arrived at by a Symposium on the Endemiology of Cancer of the Lung held by the Council for the International Organizations of Medical Sciences at Louvain in July, 1952, was a statement of belief that a significant part of the apparent increase is absolute. In England and Wales the graph of death rates shows no sign as yet of levelling out, some 13,000 deaths having been registered in 1951.[1] It may be true that a large proportion of the cases now being certified would not have been diagnosed if they had occurred 10 years ago, but the fact remains that, out of any random sample of 400 men now aged about 55, at least 10 must be expected to die of lung cancer within the next 20 years, in comparison with 200 from all other causes, even though death rates remain at their present level. This merits serious attention, and it is well that the studies initiated by the General Register Office and Medical Research Council are yielding results of great importance, unpopular though they must be.

Dr. Richard Doll and Professor A. Bradford Hill published in this *Journal* two years ago[2] a first report of an inquiry, most carefully conducted among 2,475 patients in 20 London hospitals, leading to the conclusion that "smoking is a factor, and an important factor, in the production of carcinoma of the lung." Their results were confirmed in almost all respects by a similar study of 684 cases of bronchogenic carcinoma by Wynder and Graham in the U.S.A.[3] In the opening pages of this issue Doll and Bradford Hill report the results of an extension of their inquiry during 1950 and 1951 to patients in Bristol, Cambridge, Leeds, and Newcastle-upon-Tyne hospitals and a continuation of it in eight of the London hospitals. The method of investigation, described in the first paper, was to obtain notifications of patients admitted to hospital with cancer of the lung, stomach, and large intestine, who were then questioned about tobacco-smoking, and to match each lung-cancer case with a patient of the same sex and age group suffering from a disease other than cancer. In the extended inquiry the almoners visited the provincial hospitals at intervals and interviewed patients with suspected cancer of lung who happened to be in-patients together with matched control patients having other diseases. The final classification was usually based upon the diagnosis at the time of discharge from hospital. In addition to obtaining the history of tobacco-smoking, the almoners asked questions about the proximity of gasworks, methods of heating, places of residence, and previous history of respiratory diseases.

This second report is based upon the whole series from the start of the investigation. It now comprises 1,488 patients with carcinoma of lung, of whom 1,465 were paired with control patients having diseases other than cancer, and another control group of 1,278 which included patients suffering from cancer of the stomach and the intestine. Comparison of the 1,465 patients suffering from lung cancer with their matched controls showed no significant social class differences; but there were fewer resident in Greater London (791, compared with 900 among the controls), more resident in other urban areas (500, against 394), and fewer resident in rural districts (155, against 164). Since tobacco consumption is rather greater in London this inequality would tend to reduce any excess in usage of tobacco by the lung-cancer group rather than exaggerate it. In the interviews with some pairs of patients questions about brands of tobacco, filter-tipped cigarettes, petrol lighters, and cigarette-holders were added to those described in the first report about frequency, quantity, and duration of smoking. Non-smokers were defined, as before, as persons who had never consistently smoked as much as one cigarette a day for as long as one year. Among the various quantitative measures of smoking employed were the most recent amount smoked, the maximum amount ever smoked regularly, the estimated total amount ever smoked, and the average amount smoked daily over the 10 years preceding illness, and of these the first and last were judged to be the best.

1 See *Journal* p. 1316.
2 *British Medical Journal*, 1950, **2**, 739.
3 *J. Amer. med. Ass.*, 1950, **143**, 329.
4 *Brit. J. Cancer*, 1952, **6**, 99.
5 *British Medical Journal*, 1952, **2**, 710.
6 Ibid., 1952, **2**, 982.

Among 1,357 men with lung cancer only 7 (0.5%) were non-smokers, compared with 61 (4.5%) among the same number of control patients with other diseases; and at the other extreme 25% had smoked 25 or more cigarettes a day (or the equivalent in pipe tobacco), compared with 13% of the controls. Among 108 women with lung cancer 37% were non-smokers, against 55% of the controls; and 11% had smoked 25 or more cigarettes a day, against only 1% of the controls. The figures for patients in Greater London interviewed during 1950–1 agreed closely with those for 1948–9 which were analysed in the first report. In men the contrasts between smokers and non-smokers were similar in the provincial centres to those in London. From the 28 women seen in the provincial towns no conclusion could be drawn. Estimated death rates for Greater London in groups of men who had smoked different quantities of tobacco —calculated from the patients not suffering from cancer as a basis for smoking habits in the population as a whole—indicated that mortality from lung cancer may increase in approximately simple proportion with the amount smoked.

No appreciable differences were found between patients with lung cancer and other patients in the regular use of petrol lighters (43 and 41%) or of hand-rolled cigarettes (21 and 19%). Rather fewer patients with lung cancer had ever used a cigarette-holder regularly (5%, against 12%), and only three out of 504 had smoked filter-tipped cigarettes, compared with 15 out of 467 controls. Though inconclusive by themselves, these differences point in the same direction as does the finding that among men with lung cancer a lower proportion of smokers had smoked only pipes (4%, against 7% among the male controls who smoked), suggesting partial removal of an active agent before it reaches the respiratory tract. Analyses of the answers to questions about proximity of gasworks to the home and use of coal or gas in living-rooms showed no appreciable differences.

Rather fewer of the patients with lung cancer lived in the country; but the difference does not appear to be large enough to account for the observation by Stocks[4] that county-borough death rates of males were more than twice those in rural districts for the country as a whole during 1940–6, and that London rates were two and a half times those of rural districts during 1947–9. Doll and Bradford Hill conclude in this connexion that "it would seem likely that some agent other than tobacco (present perhaps in domestic chimney smoke or in the exhaust fumes of cars) is at least partly responsible for the excess mortality in towns." The percentages of non-smokers deduced from the control patients resident in Greater London, county boroughs, other urban districts, and rural districts were, after correction for the differing age distributions, 5.1, 6.8, 8.4, and 10.4 respectively, and the percentages of smokers of 25 or more cigarettes daily were 14.6, 9.9, 8.9, and 7.7, but the proportions smoking 5–24 cigarettes daily showed no consistent difference according to urbanization. Those who smoked only pipes contributed 10% to the smokers in rural districts, however, compared with 5% in Greater London.

Where do we go from here? Statistics, it is said, cannot prove causation, but neither could Koch's postulates, although the lives of millions are affected and controlled on the assumption that they have established beyond question the causative agents of certain infective diseases. All that these things can do is to show that the probability of a causative connexion between an agent and a disease is so great that we are bound to take what preventive action we can, accepting the theory as though the proof were absolute until further research leads to some modification. It would seem that such a position has now been reached with lung carcinoma, in that tobacco has been incriminated as the vehicle conveying an agent responsible for a large proportion of the cases. The nature of the carcinogenic agent is not yet known: benzpyrene has not been found in tobacco, and though the arsenic known to be present in most brands of cigarettes has been suspected there is as yet no evidence to incriminate this. Intensive research on the chemical constituents of tobacco and of tobacco-smoke is now needed, and it is surely incumbent upon the tobacco manufacturers to do this. It is a reasonable expectation that if the carcinogenic agent can be isolated it can also be removed, so that smoking will become a less dangerous occupation than it appears to be now. In the meantime the younger generation will have to decide, each for himself or herself, whether the additional risk of contracting lung carcinoma is worth taking. For a middle-aged man lung cancer diminishes his expectation of living 20 years by about one-twentieth. The apportionment of responsibility for that to smoking and other factors such as atmospheric pollution can be roughly estimated, since the statistical pieces of the puzzle now seem to fall into place fairly well and make sense. If the annual total of deaths of men from lung cancer is taken as 11,000, of whom seven out of each 1,357 would be non-smokers, the total male non-smokers dying annually would be 56; and if the proportion of non-smokers in the population at the relevant ages is taken to be 5%, the remaining 95% would also be exposed to the same risks from causes other than tobacco—which gives a total of about

1,100 deaths of men due to those causes, compared with 10,000 attributable to tobacco. By similar reasoning, with an annual total of about 2,000 deaths among women, of whom 37 out of each 108 would be non-smokers, the total female non-smokers dying would be 685, and, taking 60% of the female population at the relevant ages to be non-smokers, we can estimate that the total lung-cancer deaths of women due to causes other than tobacco would be about 1,100, as for men, the other 900 being due to tobacco. This seems to dispose of the idea that there is a sex difference in susceptibility to lung cancer, the large excess of male mortality being explicable by greater use of tobacco among men.

These are tentative estimates which may have to be modified when the British Empire Cancer Campaign has completed its field study of cancer of the stomach and other organs in North Wales, the Liverpool hospital region, and the Isle of Man.[5] The large apparent urban excess of lung-cancer mortality, and its correlation with size of town,[4 6] is not fully explained by the apportionment suggested above, and it may be that continual exposure to atmospheric pollution by a carcinogenic substance such as benzpyrene lowers the threshold of resistance to tobacco smoking. In that case the total contribution of atmospheric pollution to the deaths would be greater than appears from these estimates. But whether that is so or not, there is now enough evidence to justify much more energetic research into the harmful constituents of the air of towns. For more than a century the General Register Office has called attention so often to the high death rates from respiratory diseases in our northern towns that we tend to accept this as a natural phenomenon. Is it not time that abatement of atmospheric pollution was added to the regular responsibilities of public health departments instead of being left to a few enthusiasts regarded rather as troublesome cranks by the Ministry of Health?

ABUSE OF ANTIBIOTICS

The letter from Mr. Norman C. Lake in this issue (p. 1307), protesting against the "unthinking universal employment" of chemotherapeutic agents, calls attention again to a trend in present-day therapy which merits serious consideration. He cites two cases, in one of which the prophylactic use and in the other the therapeutic use of antibiotics obscured the development of serious complications. The example of therapeutic use and its consequences poses a distinct problem, and one which does not appear to have been generally recognized or adequately studied. It is understandable that partially effective chemotherapy should abate fever and improve the patient's general condition without actually arresting the progress of infection. But it is not clear why, if peritonitis still exists, it should fail to show any of the usual signs. There are no reasons for supposing that antibiotics have any action except on bacteria, and in very mixed infections of this kind they often eliminate the sensitive majority, leaving a minority of resistant types which are not necessarily highly pathogenic. Whenever streptomycin is used there is always the possibility of acquired resistance, and the turn for the worse taken by the patient described by Mr. Lake may well have followed escape of bacteria from the influence of this drug, with consequent renewed multiplication. As a possible explanation of the absence of signs it may be assumed that restrained or low-grade infection fails to excite the reflexes on which these signs depend. Whatever the explanation, this warning is one which should be heeded, and further published experience of the silent progress of infection during antibiotic therapy would be helpful.

Prophylactic use of antibiotics is another matter, because it is arguable whether in given circumstances it is indicated at all. It is a common practice to give penicillin before and after a clean operation for the dual purpose of protecting the operation site against accidental contamination and of preventing chest complications. It sometimes fails in the latter purpose, and when it does so the infection developing is penicillin-resistant and consequently much more difficult to treat. It is evidently impossible to lay down hard-and-fast rules about this practice, although there are certain types of patient in whom it is clearly indicated. Penicillin cover is certainly necessary for dental extraction or tonsillectomy in a rheumatic subject. It is equally clearly indicated in operations in a septic field, where any interference may otherwise cause an acute exacerbation. This applies particularly to the surgery of infected bone, and the use not only of penicillin but of other antibiotics has greatly facilitated major operations on the lung. Operations on the alimentary tract are in a different class, since here only the normal flora is usually to be feared. The use of sulphonamides or antibiotics as intestinal antiseptics preparatory to operations on the colon is sound and established practice, but it relies rather on the local than on any general effect. There is no similar procedure for operations on the stomach or oesophagus, nor is there the same need for it, the flora of this area being much scantier and the factor of distension by gas inoperative. Whether systemic antibiotic prophylaxis is indicated in such operations may presumably depend on the features of the individual case, but in a straightforward gastrectomy the necessity for it is at least doubtful, and if there is

any marked divergence of opinion on its merits a controlled trial would seem to be indicated. As a cover for operations on the urinary tract a sulphonamide is indicated—unless some infection insensitive to these drugs already exists—antibiotics being held in reserve to deal with later developments, if any.

All these are examples of operations in fields where infection already exists or is particularly apt to develop. For most operations in healthy and bacteria-free tissues there should be no need for any such prophylaxis. In these and other circumstances, including the great majority of those obtaining in the field of obstetrics, it is certainly justifiable and probably preferable to withhold all such treatment unless and until some signs of accidental infection appear. An important advantage of this policy is that any infections which do occur are then likely to be easily controllable by penicillin. If, on the other hand, they arise in patients already being given this drug, often in an environment which can almost be described as saturated with it, they are certain to be resistant to this the most effective of all the antibiotics, and it may not be easy to find another which will serve in its place.

Mr. Lake brings a third and more general charge, particularly against the youngest generation of doctors: that antibiotics are being used indiscriminately for trivial conditions. It is by no means the first time this has been said even in this *Journal*, and authors in other journals in many countries have for some time past been urging that the prescription of antibiotics should be drastically curtailed. It is contended in particular that they should not be used for trivial ailments, as mere febrifuges or as placebos. There are many reasons for such restraint, of which the more obvious are economy and the desirability of making a diagnosis before starting treatment, particularly when the treatment is apt to obscure it altogether. Two other specific reasons have led to these protests. One is the risk of sensitization: the proportion of patients sensitized to penicillin is rising slowly but steadily, and if the treatment which produced this state was in fact unnecessary it is a pity that they should have to run serious risks on a later occasion when they really need it. A more serious reason is acquired bacterial resistance, not so much in the individual as in the population as a whole. All the newer antibiotics are slowly wasting assets by reason of this change, but if they were restricted to their proper fields of use we could enjoy them for many years longer. Let anyone tempted to use one of them for, say, a common cold reflect that this type of use may abolish its effect in a patient with septicaemia at some time in the future.

A PHARMACY CENTENARY

Pharmacy of a kind is as ancient as the human ills it is designed to soothe, but in the sense of the art and practice of collecting, preparing, and dispensing drugs the word was first used at the end of the sixteenth century. It is exactly a hundred years, however, since pharmacy acquired its legal status. This was the result of the Pharmacy Act of 1852, which first established the distinction between registered and examined and unregistered and unexamined chemists and druggists. The Act created a register of pharmaceutical chemists and committed it, with the disciplinary powers attached to any professional register, to the Pharmaceutical Society of Great Britain, which had been established a few years before. The founders of the Society were themselves chemists and druggists in the metropolis and provincial towns, and one of the purposes of the organization from the beginning was to prevent ignorant and unqualified persons from assuming the title of or pretending to be pharmaceutical chemists or pharmacists. It was incorporated in 1843, and the Act of 1852 confirmed its charter and determined the powers of its council and the rules which must govern the maintenance of its register, the conduct of its examinations, and the appointment of its examiners. One of the provisions of the Act was that no person who was a member of the medical profession should be entitled to be registered as a pharmacist, and if any pharmaceutical chemist obtained such a diploma his name was not to be on the register during the time he was engaged in medical practice. The Act was followed by amending Acts, and by the later series of Dangerous Drugs Acts and similar measures designed to safeguard the public health. It was six years after the passing of the Pharmacy Act that the Medical Act, 1858, gave the General Medical Council the right to publish the *British Pharmacopoeia* or a list of medicines and compounds with the manner of preparing them, together with the true weights and measures by which they should be prepared and mixed, and the present *British Pharmacopoeia*, published in 1948, is the seventh of the series.

Last week the Pharmaceutical Society arranged at its house in Bloomsbury Square a two-day exhibition—it might well have been extended over a longer period—of appliances, drugs, and prescriptions in use among pharmaceutical chemists a century ago. In the year the Pharmacy Act came into operation the Society was presented with a collection of about 130 specimens of the drugs used at that time, and some of these were on view; but what were perhaps more interesting were the pharmaceutical implements of the period. One of these was a plaster iron, a device whereby plaster material was warmed by gas and spread on a muslin foundation in one smooth movement. Many of the specimens in the Society's museum go back to earlier centuries, to very primitive pharmacy indeed, and it was against this background that the mid-nineteenth-century pharmacy was to be seen. Pharmacists have always taken an immense pride in their art, and to the products of old-time pharmacy especially a certain elegance attached itself. No wonder that pharmacists have been jealous of their craft.

THE HEALTH OF THE ARMY

It is good to see in the recent *Report on the Health of the Army, 1946–1948*, a return to the old-established custom of publishing a comprehensive résumé of the work done by the medical services of the Army, though it is to be hoped that subsequent reports will reach the printers nearer to the date of the period covered. In such a highly organized Service as the Royal Army Medical Corps there are opportunities for planning and research which are often denied to other less well equipped branches of medicine. The report gives an excellent account of the birth of the new system of medical classification known as the Pulheems system.[1] Although primarily designed to meet the needs of the armed Forces, it has been suggested that this classification, or a modification of it, might be used for the placing of industrial workers in suitable jobs.

Since its inception the Royal Army Medical Corps has striven to prevent illness, and its record in many wars shows how successful the Corps has been. In fact war has given Army doctors opportunities which years of peace could not supply, and now such conditions as malaria, scrub typhus, and septic infections in traumatic injuries, to mention only a few, can be controlled to an extent unthought of previously, and it is not only the fighting soldier who has benefited but the entire world. The title of the Director of Hygiene has now become Director of Army Health, and in other ways too the Army Medical Service continues to emphasize positive striving for health: for instance, educational courses are held for both officers and other ranks in all branches of the Service, including the Women's Services. In looking for ways to improve the standards of physical and mental efficiency the R.A.M.C. very wisely invites the co-operation of civilian scientists, and eminent physiologists and other experts are now serving on the re-established Military Personnel Research Committee.

The report, which covers the years immediately after the war, shows the changes brought about by National Service. There is now a large Army composed mainly of men with a comparatively short active service liability, and the movement of men in and out of the Service is constant. This affects all branches of the Service, including the R.A.M.C., and places a great strain on the medical service and in particular on the regular officers of the Corps. If the regular cadre of medical officers was fully up to strength these difficulties would be much less, but unfortunately the Corps is very short of regular officers, particularly specialists. In fact the problem of finding enough surgeons for the Army is almost insuperable. Contrary to what has been said in other places, the young National Service medical officer has, by and large, good professional experience, but from the nature of things he cannot be expected to be a specialist or to have the same knowledge of military medicine or administration as his regular colleagues. If a high standard of medical care is to be maintained in the Army the conditions of service of regular officers in the Corps must be such as to attract and retain young, well-qualified doctors into the Service. It is to be hoped that the Minister of Defence will be able soon to approve an acceptable scheme, lest the difficulties now so apparent reach a stage where no solution is possible and the R.A.M.C. finds itself in a position in which it can no longer render the valuable and essential service it has so proudly provided in the past, both in peace and war.

[1] Fletcher, R. I., *British Medical Journal*, 1949, **1**, 83.

CORTISONE IN ALLERGIC RHINITIS

Vasomotor rhinitis, or perennial allergic rhinitis, is one of those minor but distressing complaints for which no certain cure is known. The symptoms—uncontrolled sneezing followed by profuse rhinorrhoea—are probably caused by an allergic reaction of the nasal mucous membrane to various protein dusts; but treatment by specific desensitization is often disappointing, and response to antihistamine drugs is unreliable. Vasoconstrictor drugs applied locally or systemically may temporarily suppress symptoms but rarely give very lasting benefit, and avoidance of the many allergens responsible for the disorder is scarcely compatible with normal life. Many allergic diseases are known to respond favourably to treatment with cortisone and A.C.T.H., and recently these drugs have been used in the treatment of allergic rhinitis. A few weeks ago Mr. J. P. Stewart, in his presidential address to the Section of Laryngology of the Royal Society of Medicine, described the results he had achieved in using these drugs in 33 patients with allergic rhinitis. The efficacy of treatment was judged by clinical improvement and by comparing the microscopical appearances of the nasal mucosa obtained by biopsy before and after treatment. In almost all patients given systemic treatment the initial improvement was rapid, symptoms sometimes disappearing completely after the first day's treatment. Unfortunately symptoms often returned when treatment was stopped, and some patients relapsed while on a maintenance dose. Topical application of cortisone and A.C.T.H. failed to give constant relief of symptoms. Mr. Stewart concluded that treatment with cortisone and A.C.T.H. was effective and safe in selected patients, but he deprecated the indiscriminate use of these agents.

The effect of cortisone and A.C.T.H. in allergic rhinitis was first noticed by Carryer and his colleagues[1] when using these drugs in the treatment of asthma. They found that those patients who had associated vasomotor rhinitis often obtained relief from their nasal symptoms while under treatment. In the hope that cortisone might cure allergic rhinitis, extensive trials were undertaken in patients suffering from the disorder, and Williams[2] has recently summarized the results. He concluded that the early hopes that cortisone would prove an effective measure in allergic rhinitis have not been fulfilled. Although there is no doubt that most cases will respond favourably to the initial course of treatment, it seems that a second course is less active than the first, and most cases respond hardly at all to subsequent treatment. The patient with allergic rhinitis may well find a good linen handkerchief of more lasting comfort than cortisone.

[1] *J. Allergy*, 1950, **21**, 282.
[2] *Ann. Otol. (St. Louis)*, 1952, **61**, 497.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE BACKWARD CHILD—I. PRE-SCHOOL AGE

BY

BRIAN H. KIRMAN, M.D., D.P.M.

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Mental deficiency is not a clinical entity like diabetes mellitus. There is no simple method of arriving at the decision to class a particular child as mentally defective. There is no specific medical treatment for most of the conditions causing mental retardation. In fact backwardness is often more an educational or social problem than a strictly medical one. Nevertheless it is the duty of the medical officer of health and the school medical officer to ascertain cases of mental defect and ineducability, and the institutions in which some 55,000 persons certified as mental defectives are detained are classed as hospitals. Moreover, it is to the family doctor that the anxious parent turns when there is a delay in passing the first milestones.

Aetiology

There is no one major cause of inefficient functioning of the brain in a young child. There are hundreds. An exhaustive account of the pathology of mental deficiency would cover the whole of neurology. Children with grossly damaged brains are usually idiots (the severest grade of mental defect) or imbeciles (the medium grade). Some of these fall into easily recognizable clinical categories—for example, mongolism, hydrocephalus, microcephaly, gargoylism. In other cases the history assists in labelling the particular clinical condition—for example, rhesus incompatibility with a history of severe neonatal jaundice—in others there is a history of German measles in the first three months of pregnancy. Birth injury accounts for perhaps 5% of all cases labelled as mental defect. Very rarely nowadays is syphilis the cause of severe brain damage in the infant. Meningitis and encephalitis are more commonly to blame. In the rarer syndromes there may be a family history of brain pathology—for example, gargoylism and phenylketonuria, which are usually considered to have a recessive mode of inheritance, or epiloia (tuberous sclerosis with adenoma sebaceum), which is held to be a dominant character.

However, most children with a poorly functioning brain look much like other children. They are not distinguished by peculiar features as in mongolism or gargoylism, or by other so-called "stigmata" such as squint, abnormally shaped ears, or incurved little fingers. They are remarkable for their slowness of development. At necropsy it may be found that these unclassified idiots and imbeciles have all manner of defects of the brain—for example, porencephaly or microgyria—but the clinician can only recognize these conditions in life by elaborate methods such as air encephalography. In a few cases the diagnosis of a clinical condition—for example, mongolism—is a fair guide to prognosis.

Degree of Defect

None the less, the clinical diagnosis is of less immediate moment than the degree of defect. It is customary to attempt to measure this by means of some type of intelligence test. However, results so obtained should be treated with reserve. An intelligence quotient is much more liable to error than such a biological measurement as, for example, that of haemoglobin. There is no general agreement on the nature of intelligence, and tests which vary from those of an educational type like the Binet–Simon to those of social development like the Vineland scale often give very different results in the same patient. Even so, attempts at an objective assessment of a child's performance represent an advance on the attitude common some years ago which paid much attention to the shape of the head and pinna, the set of the eyes, and other items of physiognomy which bear little relation to mental capacity. Those who are often consulted about backwardness in children should be familiar with the technique of the common tests, otherwise they may find themselves accepting as final a decision based on an arbitrary I.Q. In general, however, tests are even more unreliable when used by the medical practitioner who has only rare occasion for their use than when applied by the experienced psychologist.

Progress

The severe grades of mental deficiency are fortunately the least common. Idiocy is relatively rare. The practitioner is most likely to be consulted about children who are a little less forward than their brothers and sisters or the child next door. His main task may be to allay the undue anxiety of the parents. In any prognosis which he may make before the age of 5 he should state that it is only tentative and subject to revision. Definite predictions are always unwise and usually wrong.

In order to assess prognosis when a child is, for example, slow in getting on to his feet, one should remember that the brain will develop even if it is a faulty inferior organ. Even an idiot goes on developing mentally up to the age of 16 or over. It may not be much, it may be only to feed himself with a spoon, to be continent of urine and faeces, or to dress himself. None the less, that part of his brain which has escaped injury matures and develops at a rate parallel to, though below, that of the normal organ. Therefore the possibilities of development in any young child, no matter how behind he may seem, are considerable.

There are a few forms of mental deficiency in which the patient gets progressively worse. Fortunately all of these are rare—amaurotic family idiocy, Schilder's disease, juvenile G.P.I. Most general practitioners never see such a deteriorating case. They are the exception to the general rule, which is that severe mental defect is due to damage to the brain, occasionally hereditary, usually before birth—damage which leaves an inactive scar or defect.

Maladjustment

There are, however, many backward children, perhaps the majority, in whom the defect is functional and perhaps only temporary. The term "maladjusted" has come into fashion of late to describe children presenting a wide variety of signs of psychological disturbance ranging from normal naughtiness to severe mental illness. Not all maladjusted children are backward. Some may be found very forward but give their parents ground for anxiety in other respects. However, maladjustment may lead to backwardness. Maladjustment is a relative term. It means that the child does not fit into his particular environment. A minority of relatively bright children find their way into mental deficiency institutions, children who have sufficient capacity to have managed at school had their circumstances been more favourable. Most of these children are illegitimate, homeless, or, occasionally, from bad homes. They are thus emotionally deprived, to use another term in current vogue. They have been pigeon-holed as defective because of their difficulty in fitting into the very rigid standards laid down by institutions such as nurseries. An

appearance of lack of mental capacity is readily produced by any form of emotional disturbance. Simple shyness is the best and commonest example. The difficulty is not overcome by the application of standard tests, since, however tactful and charming the examiner, the child may be too inhibited in the presence of a stranger to co-operate.

Where emotional upset is suspected to be the cause of the delay in development, treatment should aim at an alteration of the environment. Play therapy, when practicable, achieves this by providing opportunities for personal contact and self-expression hitherto lacking. Loneliness and over-protection of an only child may lead to severe disturbances. This is most common in surburban type surroundings and can be best overcome by opportunities for mixing such as are provided in the day nursery or recreation ground. For the emotionally deprived child with no suitable home of his own, the foster-home is the best solution.

Infantile Psychosis

Severe emotional disturbances are rare in children, but a diagnosis of infantile schizophrenia is fashionable, especially in America at the present time. This is largely because parents with a severely handicapped child are reluctant to admit that the lesion is permanent and irreversible. Some idiots do remind one of adult schizophrenics, but there is no proof that the condition is due to similar factors. In any event there is no general agreement on the cause of adult schizophrenia. Cases of this type in children do no better than other mental defectives, and often do worse.

Special Defects

Backward children are not usually retarded in some particular faculty. They are commonly below par in every way, often physically as well as mentally. They are deficient in height and weight and look younger than their years. A severely affected child of 4–5, for example, may look like a baby of 18 months, just able to walk, but unsteadily, without speech, doubly incontinent, and barely able to use a spoon. Such a child seldom presents the bizarre features encountered in adult mental illnesses. Further, he is to all intents and purposes a child of 18 months. If he is treated as such difficulties seldom arise. Few mothers, however, can adjust with equanimity to the notion of such a perpetual Peter Pan. In mental defect, usually the motor, sensory, conceptual, and emotional accomplishments are all equally delayed. Thus, slowness in walking is accompanied by slowness in recognizing people, by slowness in understanding instructions, and by delay in forming strong emotional attachments to parents or others. An understanding of this fact will help us to pick out those children who are classed as mentally defective because of some specific defect. A good example is the partially deaf child. Such a child may learn to walk at the usual age, be quick, active, and show much ingenuity in his play. On the other hand, he will be slow in learning to speak and in understanding verbal instructions. His character may suffer from lack of appreciation of his difficulty and he will become solitary, preferring his own company to that of others. His deafness makes him difficult to control and rebuke, so that he acquires a reputation for being naughty, wilful, wayward, difficult, destructive, spiteful, and bad-tempered. He may then well be labelled intellectually dull if his auditory defect is not recognized. Partial deafness, particularly high-tone deafness, is, naturally, more apt to be missed than complete absence of hearing. If the defect is recognized early the harm can be undone by special methods of education and speech therapy appropriate to the deaf.

Defects of vision are less likely to cause confusion, but blind children who could have been educated by special methods are occasionally encountered among mental defectives. Even cleft-palate with attendant speech difficulties may lead to an underestimation of intelligence.

Perhaps the biggest group of children with special handicaps apt to be confused with general mental defect is that suffering from cerebral palsy. Much publicity has recently been directed to this problem, and parents are often relatively well informed about it. However, much confusion still exists. Parents of a child who has perfectly normal or even subnormal muscle tone will cling to the belief that it is spastic and can be cured by physiotherapy. On the other hand, there are some hundreds of patients with spastic diplegia, athetosis, chorea, certified as ineducable at an early age, although potentially intelligent. This is not surprising, for the child with Little's disease looks like an idiot. He grins from ear to ear, drooling saliva, and his utterance is so thick that it is intelligible only to those who are willing to listen with patience and attention. If he walks, his gait is unsteady. Having failed a Binet type test because of his faulty articulation he also fails a performance test because of poor muscular control. Yet it is well known that a few individuals so affected are capable of considerable intellectual attainment. Others, even more remarkably, accomplish fine handiwork. Children with cerebral palsy are properly classed neither with the physically normal nor with the mentally handicapped. If of sufficient intelligence they need a specially designed curriculum in a special class. Existing provision is quite inadequate, though a few groups under pioneer workers have achieved outstanding success.

In mentioning these special defects it should not be assumed that all blind, deaf, or crippled children are of normal intelligence. The same process, whether it be environmental—for example, maternal rubella—or genetic—for example, cerebromacular degeneration—may, in addition to damaging the brain as a whole, also affect special organs—for example, the ear or eye. Thus a number of children have multiple defects and have both general mental deficiency and special handicaps. This consideration accounts for the fact that among cases of severe mental defect there is a somewhat greater proportion of physical abnormalities such as microphthalmia, malformed pinna, talipes, spina bifida, malformations of the digits, etc., than in the general population. Hence the term formerly in use of "stigmata of degeneration."

Caution in Diagnosis

A diagnosis of mental deficiency should never be made on the basis of one examination. In this respect the family doctor has a great advantage over the paediatrician, the medical officer of health, the psychiatrist, and others who may have very limited opportunities for observation of the child. Any decision should take into account the physical health of the patient—repeated physical illnesses may produce temporary mental dulling—and the family background. Since there is no specific treatment there is not the same virtue in making a diagnosis of mental deficiency as with specific medical entities. In borderline cases the diagnosis is better not made—at all events before the age of 5.. There is no value in alarming the parents unnecessarily; and for many the words "mental deficiency" have a most disturbing effect. Many members of the public fail to distinguish between insanity and simple-mindedness, and not all members of the medical profession are clear about the difference between disorder of the mind with the unpredictability of behaviour which it involves on the one hand and failure of development of the mind on the other. Thus they are not always in a position to explain to a parent that a child affected by the latter condition will always be simple, childish, and easily led, but, apart from this, need not necessarily be more trouble than the normal child.

In the few cases in which physical deformity is obvious—for example, mongolism or microcephaly—the medical adviser may reach a decision on the presence of deficiency even at birth. There is no advantage, however, in prematurely informing the parents of the condition. They are likely to make a better adjustment if they are allowed gradually to discover the child's disabilities for themselves. Particularly in cases in which there is any doubt is delay in voicing an opinion desirable. The more normally the

child is treated the better are his chances of normal development. It should be recognized that mental deficiency, viewing the condition psychologically rather than legally, is very common. In fact most people with very limited intellectual capacity are not labelled as defectives but fit into the general community and remain as ordinary citizens. The Wood Report* put forward the view that some 300,000 should have been recognized rather than the existing figure, which has fluctuated around 100,000, only half of whom live in institutions. This suggestion was made on the supposition that it would be possible to provide a more adequate educational service for the educationally subnormal (E.S.N.), who were at that time certified as feebleminded under the Mental Deficiency Acts. Unfortunately this hope has not yet been realized, and there are still some 25,000 E.S.N. children competing for 18,000 places. At the present time ascertainment as mentally defective is a definite disadvantage for a borderline case, since it implies exclusion from the educational system.

Certification

Certification as mentally defective is a very serious step, similar to certification as insane. In practice experience has shown that once a child has been certified as mentally defective he is quite likely to be confined in an institution for the remainder of his life. There is no provision for defectives similar to that under the Mental Treatment Act whereby treatment and assistance can be obtained on a voluntary basis without loss of civil rights and the other legal consequences of certification. In practice, then, at present, certification should be limited to those whose condition is such that it is impossible to deal with them through the other social agencies and who must be separated from society at large for the purpose of special supervision and treatment. The medical officer of health of the local health authority, which has the duty of ascertaining mental defectives, will usually be ready to give advice in cases of doubt or difficulty.

Admission to Hospital

Parents sometimes approach mental deficiency as they would any specific medical problem. This attitude may lead them to seek admission to hospital with a view to curing their child's deficiency by surgery, shock therapy, psycho-analysis, or by some other method which they imagine will remedy the condition. It is necessary for the doctor to explain that the most that can be got from an institution is training and education. In some parts of the country it is exceedingly difficult to obtain institutional care for mental defectives, though the provision in Britain is better than in many other countries. Institutions are handicaped by a grievous shortage of nursing and other staff. They perform an essential task in caring for those children who cannot possibly be looked after at home. It should, however, very seldom be represented to a mother that a child will progress better in a hospital for mental defectives than at home. In fact the reverse is the rule. At home the child normally receives a good deal of attention from the mother even if she has other children, whereas in an overcrowded and understaffed hospital the staff may find it difficult to do more than care for the child's immediate needs. Accordingly speech and other attainments usually progress more rapidly at home than in the limited institutional environment. Physically, too, a young child usually does better at home than in hospital. The hazards of infection are not so great, whilst a firm emotional attachment in most homes contrasts with the impersonal institutional atmosphere. This latter factor often leads to feeding difficulties and loss of weight when a child is first removed from home.

For these reasons, unless the home is unusually bad, admission to hospital for a young mentally defective child should only be sought in the interests of other members of the family. The higher the income the easier it is to make provision for a mental defective at home. On the other hand, if a numerous family is living under overcrowded conditions, perhaps in one room, the difficulty of coping with a low-grade defective may be very great. If the mother is in poor health her task may be very difficult. The attitude of the parents is all-important (as is that of the neighbours). Many superstitions attach to mental defect as to insanity. Previous exaggeration of the role of syphilis may have been a factor in this. The same applies to alcohol. Guilt may be experienced by the parents in connexion with an attempt at abortion, though this is rarely a cause of mental defect. Sexual aberrations may also be blamed for the abnormality. Thus a strong sense of shame, mixed with resentment, is often experienced by parents. It is easy to understand why mutual recrimination leading to open rupture may develop between the parents. The advent of a defective child not uncommonly leads to the break-up of the family, a process which is hastened when the relations on either side take an active part in fault-finding, and a critical scrutiny of the genealogy. It is the duty of the medical adviser to explain that mental deficiency is due to disease of the brain for which neither parent is to blame and which is usually not simply inherited.

The degree of the defect is also important in deciding admission to hospital. It is unreasonable to expect a mother to nurse the grosser cases of hydrocephalus and microcephaly, but there is less often reason why a mongoloid baby should not be cared for at home, at least for the earlier part of its life.

Educability

Legally, the question of educability is one for medical opinion. The medical man is, however, ill advised to rely solely on his own judgment. The person who has to do the job of teaching is the teacher. It should therefore be very exceptional for a child to be certified as ineducable before the teacher has formed an opinion. Apart from exceptional cases the issuing of certificates of ineducability under the age of 5 is to be deprecated.

Ineducability is of course a very artificial notion. Even an idiot can learn something, and the majority of ineducable children are far from being idiots. Some are certified as feebleminded on the basis that, although not imbeciles or idiots, they are incapable of being educated with others; there is usually a history of temper tantrums or aggressiveness in such cases. Most local authorities—whose responsibility the care of the defective child in the community is—have recognized the fact that the mental defective is educable after a fashion by setting up occupation centres which these children attend daily. The curriculum in these centres, which aim to have classes of not more than 15, is very similar to that in a special E.S.N. school which is attended by the educationally backward (children classed as feebleminded before 1944). In the interests of the imbecile or feebleminded child such an arrangement whereby he can live at home but attend daily at a centre is ideal. Unfortunately, in many cases there is no such centre or the existing one is too small.

If, then, the child with a medium degree of mental defect has the good fortune to have a suitable home and parents who are able to accept the fact of his disabilities with reasonable philosophy, there is no reason why he should not remain in the community to grow up with his more gifted brothers and sisters. Difficulties may arise at later stages, but these are similar in nature to the hazards which any child may encounter.

Part II will appear in our next issue.

*Report of the Mental Deficiency Committee, 1929. H.M.S.O., London.

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Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Abuse of Antibiotics

SIR,—To decry the life-saving value of the various antibiotics and sulphonamides which the genius of the bacteriologist, the chemist, and the biochemist has placed at the command of the clinician would be both stupid and ungracious; I hope therefore that the purport of this letter will not be misunderstood.

It would seem that certain dangers arise from the very efficiency of these materials, in the same way that dangers are associated with the indiscriminate use of morphine because of its unequalled power of relieving pain. We warn our students, for instance, against the employment of morphine for the relief of abdominal pain unless a diagnosis has been reached and appropriate rational treatment decided upon, in the fear that the drug might otherwise obscure important signs and symptoms and so lead to fatal delay in instituting such treatment. Yet these new powerful materials, equally capable of hiding symptoms, are being given indiscriminately without thought of this aspect, and often for what is called prophylaxis. Naturally, I view these matters from a surgical angle, but it seems probable that the same remarks would apply to medical cases.

I leave the bacteriologists to explain why a patient who has had an abdominal operation, say a gastrectomy, can, while under the influence of doses of antibiotic which would have been considered fantastically large in earlier days, develop, without signs or symptoms, and thus completely unsuspected, a large collection of pus under the diaphragm. Furthermore, why, when the abscess has been belatedly discovered and the aspirated pus proved sterile, does the abscess spread and the pathological process continue until adequately drained? Bacteriostatic instead of bactericidal effect may be the answer—I don't know, but the facts are incontrovertible. Several cases of this nature have been brought to my notice.

The most recent example which prompted this letter is instructive. A youth was operated upon for a ruptured appendix which had produced a truly general peritonitis. The peritoneal cavity was completely emptied of pus by suction, the very adherent and buried appendix was left, and the abdomen drained. He was immediately placed upon fairly large doses of penicillin and streptomycin. His immediate progress was extraordinarily good and rapid. Within three days he was apparently quite well, temperature and pulse normal, abdomen soft, feeling excellent, and taking food with a relish. Indeed, his discharge had been arranged, when, on the 13th day, he suddenly became very ill again, with rise of pulse, vomiting, and rigidity. A second laparotomy revealed an enormous number of collections of pus between matted coils of intestine, some of which had obviously been present for many days. I cannot believe that careful observers would not have detected that the peritonitis was persisting had the signs and symptoms not been hidden by the antibiotics, yet I realize to the full that the patient might not have survived to have a second drainage if the antibiotics had not been given.

This letter, therefore, is not a warning against the use of antibiotics and similar materials, but against their unthinking universal employment. One hears nowadays of operations being performed "under an umbrella of antibiotics." I don't like the metaphor, because umbrellas can obscure the sun as well as keep off the rain. To listen to some of our recently qualified doctors one would get the impression that no one recovered from infectious illnesses before the introduction of these new medicaments. In the casualty departments of hospitals particularly they are too lavishly used for quite trivial cases.

This, Sir, seems to me to be an abuse of some of the most valuable materials which the outcome of inspired research has placed in our hands. I hope that some restraint will be exercised in their employment in such circumstances, and that it will be realized how completely they may obscure, in certain instances, the development of quite serious complications.—I am, etc.,

London, W.1. NORMAN C. LAKE.

Antibiotic Treatment of Tuberculosis

SIR,—In his paper (November 8, p. 1015) Dr. F. J. W. Miller indicates that specific treatment by anti-tuberculous drugs is seldom necessary in children with uncomplicated primary intrathoracic tuberculosis—a condition which generally heals spontaneously. In the very young age groups and in others in whom familial infectivity continues, or where home conditions are bad, it is necessary, of course, to advise treatment in an institution and in selected cases to treat actively by antibiotics. Dr. Miller's advice is timely, since, in our experience, many primarily infected children are given streptomycin as soon as the diagnosis is made, and a long-term stay in an institution is advised irrespective of other considerations, the often detrimental effects of separating the young child from its home being forgotten.

Cases of adult type pulmonary tuberculosis, too, are not infrequently treated and advised in this indiscriminate way. In a recent paper[1] we pointed out the disadvantages of precipitate treatment in making a plea for the more conservative treatment of pulmonary tuberculosis in suitable cases where, in our experience, spontaneous retrogression is prone to occur. The dangers of administering the appropriate antibiotic drug almost as soon as the diagnosis is made were stressed by us, particularly the disastrous consequences of drug-resistance to the sufferer, to the public, or to the patient's home contacts and attendants, who may become infected by streptomycin-resistant tubercle bacilli. Much cost to the National Health Service could be saved by a more judicious selection of cases suitable for treatment by expensive antibiotics. The present fashion to prescribe without qualification the appropriate antibiotic in tuberculosis is to be deprecated. In tuberculosis the good results often obtained by long-continued bed rest alone are apt to be forgotten. In three groups of cases—"localized miliary tuberculosis," "cavitation complex," and "right upper lobe complex"—natural unaided recovery is to be expected, and we have recently published[2] the results of treating these types conservatively and have presented radiological evidence illustrating their proneness to healing. Once the tendency is recognized and accepted in these three groups and in the primarily infected child with whom Dr. Miller deals in his paper, some of the risks and sequelae of unrestricted antibiotic therapy in tuberculosis may be reduced if not avoided entirely.—I am, etc.,

Hull. LASAR DUNNER.

REFERENCES
1 Dunner, L., and Hicks, M. S. (1952). *Tubercle (Lond.)*, 33, 308.
2 —— (1952). *Acta tuberc. scand.*, 26, 363.

Specialists in Physical Medicine

SIR,—The point which Sir Max Page (November 29, p. 1203) makes, that prolonged physiotherapy treatment is often prescribed for minor injuries and osteoarthritis, is a valid one, but I venture to suggest that this is more likely to apply in hopitals where no physical medicine specialist is in charge of the department. Where there is inadequate supervision of these departments, patients tend to continue indefinitely upon treatment which at most is giving but temporary relief. Physical medicine specialists know the limitations of their specialty more than specialists of other departments, and it is my practice never to continue treatment which is not actually improving the condition.

Unfortunately specialists in other branches order treatment in a vague way, leaving the physiotherapists themselves to choose the details and duration of treatment. The departments are so often used as a convenient place for disposal of difficult patients. These are the chief ways in

which physical medicine departments are abused, leading to wastage of time for both patients and physiotherapists. I therefore support Lord Horder's plea for more physical medicine specialists, and also plead for more co-operation from the other departments in the proper use of physical medicine.—I am, etc.,

London, W.1. ALAN STODDARD.

SIR,—Sir Max Page (November 29, p. 1203) must have been singularly unfortunate in his contacts with physical medicine if his acquaintance with the practical workings of physiotherapy clinics causes him to labour under the impression that a "passive attitude towards the process of recovery" dominates modern physical medicine. The emphasis has so insistently and for so long been on the achievement of optimum restoration of function through planned activity that it is difficult to understand how the change in character can have escaped his notice.

If my reading of Lord Horder's letter (November 15, p. 1095) is correct, he pleads for the creation of additional posts in the trainee grade "to maintain the number of consultants in this field at an adequate level. . . ." I fail to find there any hint of sinister designs to produce more consultants in physical medicine with a dog-in-the-manger attitude, scanning the medical field for new spheres of interference and encouraging the physiotherapist to "be regarded as a universal healer." On the contrary I read into it a desire to see the specialist in physical medicine "take an honoured place in the service of medicine. . . ."

It is a pity that Sir Max should have based his critical remarks on a conception of physical medicine which has long since been disowned by reputable medical men who practise physical medicine at a time when a sincere effort is being made to improve the physical medicine services and their relation to medicine. The pity is all the greater as I am convinced that this is precisely what Sir Max would wish.—I am, etc.,

London, W.1. PHILIPPE BAUWENS.

SIR,—There may be something in Sir Max Page's suggestion (November 29, p. 1203) that long courses of physiotherapy in certain cases are not necessary or, in fact, desirable. But surely that is a very sound argument in favour of having a full-time physical medicine specialist in every large physiotherapy department. He would see every patient sent to the department, advise as to treatment, judge the effect on the patient, and decide the length of the course. He would work in collaboration with the referring physician or surgeon, who has neither the time nor the inclination for close supervision of treatment which Sir Max rightly says is so advisable.

As to the specialist tending to "magnify the importance of his own subject and to enlarge his department," this is almost impossible in these days of boards, committees, subcommittees, and so forth. And, anyhow, he does not recommend the patients, they are sent to him by the consultant. —I am, etc.,

Bristol, 2. A. T. SPOOR.

Test for Occult Blood

SIR,—With reference to Dr. Aneurin Hughes's paper (November 1, p. 970) and the following correspondence, may we be allowed to draw attention to an important factor which does not appear to be sufficiently appreciated? Dr. Hughes does not specify the batch of benzidine he has been using for his tests, nor is the grade of benzidine used stated in some of the recent publications on this subject. The different batches and grades of benzidine now on the market and used for occult blood tests do, however, vary widely in sensitivity as compared with the Analar grade. This has been borne out by a series of controlled tests performed in this laboratory, using different batches from several sources, but identical technique. Some batches showed even a fivefold decrease of sensitivity compared with Analar. The latter, unfortunately, is no longer produced in this country, apparently due to the fact that at one stage in the process of purifying to Analar specification benzidine assumes highly carcinogenic properties.

The position at present appears to be that some laboratories are still using stocks of Analar benzidine, while others use that now supplied "for blood tests." This obviously introduces some confusion into the already controversial subject of evaluation of methods used for occult blood tests. It is quite conceivable that workers using the same method but different batches of benzidine may obtain divergent results, which in turn will influence their opinion of a given method. We have, therefore, for the last year been using Analar ortho-tolidine, stocks of which are still available. A working solution of this reagent is stable for at least two weeks. The test has been adjusted so as to give the same degree of sensitivity as obtained with Analar benzidine by the standard methods.

It is highly desirable that specification for benzidine used in occult blood tests be introduced so as to conform with a generally accepted degree of sensitivity.—We are, etc.,

J. KOHN.
London, S.W.15. T. O'KELLY.

SIR,—I have read with interest Dr. S. Lipetz's letter (November 22, p. 1149) describing the use of Gregersen's test for occult blood in emergencies. Although I do not doubt that this test can be carried out with great ease and rapidity at the bedside, I would like to point out that many false positive results may occur, unless a controlled diet—that is, excluding meat, liver, etc.—has been given to the patient for at least two days before the test is carried out.

I feel, therefore, that the sensitive Gregersen's test would be of hindrance rather than of help in such cases of emergency where an immediate diagnosis is desirable.—I am, etc.,

Bushey Heath, Herts. L. K. MANNING.

Cardiac Arrest

SIR,—We would like to make a few observations in reply to Mr. Eric M. Nanson's letter (November 22, p. 1150). We entirely agree that the essential procedure in the treatment of cardiac arrest is cardiac massage and adequate oxygenation. This cannot be stressed too strongly, and we said so several times on the first page of our paper. In cardiac asystole it is undoubtedly the most effective treatment and the most successful. In ventricular fibrillation it is also of vital importance, and to quote what we said: "Provided that adequate oxygenation is maintained and direct cardiac massage promptly initiated and maintained, shock therapy can be applied without undue haste." This covers Mr. Nanson's point about massage sometimes being all that is required. We entirely agree with this and consider that about five minutes' cardiac massage and oxygenation is worth while trying before any form of electrical defibrillation is employed. It is quite useless to expect defibrillation to occur by whatever the method employed as long as the heart is anoxic, as one of our animal results quoted exemplifies.

As regards Mr. Nanson's comments on maintaining systemic blood pressure, the figure we quoted was obtained from the femoral artery of a dog and we have not any figures on patients as yet, except in so far as they were unrecordable by the usual type of sphygmomanometer. Our suggestion was that to augment the low pressures obtainable with cardiac massage the simultaneous administration of *nor*adrenaline might be helpful. We have as yet no experience with calcium chloride on patients, but are in process of trying it experimentally, and quite agree that it may well be a useful drug under these circumstances.—We are, etc.,

IAN MCMILLAN.
London, S.E.1. F. B. COCKETT.

SIR,—Under the title "Cardiac Arrest" (November 22, p. 1150) Mr. Eric M. Nanson states that "in order to perform adequate 'cardiac massage'" it is essential to

open the chest. I do not agree that it is essential. In the last few years I have dealt with three cases of cardiac arrest. The first was a case of hypertension on whom I was about to do a Smithwick's operation and whose heart stopped in the anaesthetic room. The second case was one of intermittent claudication, and the arrest occurred during the course of a lumbar ganglionectomy. Both these occurred in hospital. The third was in a nursing-home, and occurred during the performance of cystotomy and evacuation of clot following diathermy removal of papillomata.

In all cases an epigastric vertical incision was made in the abdomen and the heart pumped via the diaphragm. In the first case some delay occurred before massage was commenced, and the arrest had lasted over three minutes. The other cases were dealt with immediately. In all these cases the heart was started again. In the first and second case a degree of coma with convulsions and followed by disorientation lasted for two or three days, but both patients are still alive and mentally normal, two years and one year after the occurrence. In the third case the heart started and was beating strongly for several minutes, and then stopped again and failed to restart.

An abdominal incision is easier and quicker, I think, and, as these are essential factors, and the heart can be started per abdomen, I am in favour of this route.—I am, etc.,

Hove. H. J. MCCURRICH.

The Diagnosis of Scabies

SIR,—Dr. Godfrey Bamber, in his excellent article on scabies (November 29, p. 1198), refers to the necessity for some degree of skill in extracting an acarus from its burrow for diagnostic purposes. A simpler method which requires no skill is to place a drop of liquor potassae on the suspected run and scrape the skin with a scalpel until the burrow is removed. The debris is examined microscopically under a low power. The advantage of this method is that even in the absence of the parasite a diagnosis can often be made by finding an egg. The only difficulty is in choosing a suitable burrow, but scrapings from any two or three spots on the sides of the fingers or wrist will usually provide at least an egg.

The author commits a slight historical error when he implies that Neilsen in 1912 was the first to use benzyl benzoate; Crocker in his 1903 edition refers to its use by Sachs and Juliusberg and describes it as "a certain curative agent, in 33% strength."—I am, etc.,

Leeds. F. F. HELLIER.

A Simple Method of Post-operative Treatment of Torticollis

SIR,—The methods used in the post-operative treatment of torticollis range from those which employ passive movements without fixation to those which employ fixation alone. Methods which employ passive movements only are hardly adequate to prevent reunion without much separation of the divided parts. Methods which rely on rigid fixation, either by some form of plaster or splinting by leather straps, are cumbersome and often inadequate. The normal action of one sternomastoid muscle is to approximate the mastoid process to the sternum. The approximation of these two bony points involves extension of the neck, inclination of the head to the side of the muscle, and rotation of the face to the opposite side and, consequently, of the occiput to the same side as the muscle. Maximum separation of the divided fragments will be achieved by the position directly opposite to this—that is, flexion of the neck, inclination of the head *away* from the side of the divided muscle, and rotation of the face to the same side as the divided muscle. The separation will be increased if, maintaining this position, traction is exerted so as to separate the sternum and the clavicle still further from the mastoid process.

The following simple method fulfils these essential conditions. After a subcutaneous tenotomy, traction is exerted

FIG. 1.—The method of traction on the arm.

FIG. 2.—The arrangement of sandbags and pillows at the head.

by skin strapping applied to the forearm and connected to a weight of about 4 lb. (1.8 kg.) suspended over the foot of the bed. The foot of the bed is raised (Fig. 1). A pillow under the occiput causes flexion of the neck. A sandbag pressed against the occiput on the same side as the divided muscle enhances the effect of the traction exerted on the arm, inclines the head away from the side of the divided muscle, and, if the pressure of the sandbag is carefully confined to the occipital region, rotates the face to the same side as the divided muscle (Fig. 2). Passive manipulation can be executed without disturbance of the apparatus.

Children tolerate this method very well, and, with careful attention to the method by the nursing staff, it proves practical and effective. No ill effects have followed the traction on the arm, which is maintained for a period of three weeks. Subsequently, fixation is completely discontinued and treatment consists in exercises with a special effort to educate the patient to overcome the habit of holding the head to one side.—I am, etc.,

Burton-on-Stather, Lincs. DAVID F. THOMAS.

Flying Squad Unit for Abortions

SIR,—It is appreciated that abortions must provide a major problem to the general practitioner, but I cannot agree with Dr. Mary A. Foley (November 15, p. 1103) that the maternity "flying squad" should underake routine evacuation of the uterus in the patient's home. While admitting that the operation can be so performed, I am sure that it is far more safely conducted in a hospital theatre. Moreover, these cases have often suffered previous interference, leading sometimes to severe sepsis and a period of considerable anxiety. This is not to say that the maternity "flying squad" should not attend abortions at all. If the patient

is not fit to be moved, there should be no hesitation in sending for the "flying squad" at once. If the patient is fit to travel to hospital, however, it is better to give 0.5 mg. of ergometrine intramuscularly and admit her without delay. Once the condition has been dealt with and all anxiety passed, the patient may then reasonably be returned to home nursing.

The question of finding a hospital bed for abortions is a different and serious matter. I have every sympathy with the general practitioner who wastes much time on the telephone because of the reluctance of hospitals to accept abortions. The solution should not be, however, to call out the "flying squad," for this is an uneconomical use of the personnel concerned and less satisfactory for the patient. The problem can be settled by the provision of an emergency bed bureau, and by instructing hospital residents that they should not waste a general practitioner's time by refusing to admit abortions when beds are available. It is admitted that waiting-lists are long in some areas, but a hospital fails in a very important duty if it discourages the admission of emergencies—abortions included.—I am, etc.,

Bristol. T. F. REDMAN.

Is Boxing Safe for Schoolboys?

SIR,—Dr. H. Crichton-Miller, in discussing (November 15, p. 1101) "Is Boxing Safe for Schoolboys?" ("Any Questions?" October 25, p. 952), refers to deviate septum, which he considers the most common form of permanent injury, and to chronic sinusitis as a dangerous sequel.

The answers to the questions which he asks are that almost all boys of 13 arrive at school with perfectly good noses, and these include those who have septa which are not absolutely in the centre or absolutely straight. I have consulted four medical officers of boarding schools representing 75 years' experience between them. They are unanimous that the majority of boys at 17 have normal noses, and this is partly because most of them start with them, and also because any cases of injury are treated forthwith. Noses certainly get broken, but more at rugger than in boxing, and cricket and hockey are sometimes the cause.

When a boy gets contusion of his nasal area with epistaxis there is generally no permanent trouble; septic haematomata are very rare. Dr. Crichton-Miller tried to make a point that, because boxing was a common English sport and that Great Britain had the honour of being foremost in promoting boxing at boys' schools, *post hoc ergo propter hoc* sinusitis is very common. There seems to be no thread of evidence in this at all, and there seems no reason why the answer to the question should be modified.

While medical officers must watch to see that no game becomes a frequent source of injury, they also must remember what Adam Lindsay Gordon said a generation ago in his poem "Ye Weary Wayfarer":

> "No game was ever yet worth a rap
> For a rational man to play
> Into which no accident, no mishap,
> Could possibly find its way."

It is usual for the answerer in "Any Questions?" to remain anonymous, and therefore I am, etc.,

"YOUR EXPERT."

Artificial Circulation

SIR,—On two occasions recently your reference to an extra-corporeal heart–lung machine has been open to misinterpretation (October 18, p. 887, and November 22, p. 1141), and, since the cost of this machine has been dependent upon both public and private funds, you will perhaps permit me to make a correct statement about it.

Dr. D. G. Melrose's heart–lung machine was planned, designed, and developed in the Department of Surgery of the Postgraduate Medical School of London at Hammersmith Hospital. The machine's experimental trials have been, and are being, conducted by Dr. Melrose and his medical and technical team at the Buckston Browne Farm of the Royal College of Surgeons by generous permission of the Council of the College and of Professor Slome.—I am, etc.,

London, W.12. IAN AIRD.

Post-epileptic Automatism

SIR,—Dr. Clifford Allen's letter (November 22, p. 1148) raises a most difficult and significant problem in medico-legal relationships. On some half-dozen occasions I have seen patients, known to be the victims of epilepsy, who have been guilty of anti-social conduct (in some cases achieving a criminal quality) which was not automatic but apparently purposive and highly integrated. In some of these cases there was very good reason to believe that just prior to such anti-social episodes they had experienced an epileptic fit. One point raised by Dr. Clifford Allen's letter depends on what connotation we give to the term "automatic."

We can only speculate concerning the nature of epilepsy, though we know something about some of its causes and we have for consideration a linear series of episodes at one end of which is coma and at the other end of which is full consciousness in a whole integrated self, deemed to be responsible at law for its actions. Dr. Allen's letter also draws attention to the necessity of an (at least conceptual) analysis of this linear series of clinical states of the self. We are here presented with Zeno's paradox, for, if we conceive of a linear series of events proceeding from coma to full consciousness, who can determine (other than arbitrarily) at what point the term "conscious" can be applied clinically, and who can determine at what point the self has been recreated with a sufficient degree of integration to establish responsibility at law? We all know that there is a "more or less" zone in this linear series, and it is in this "more or less" zone that our medico-legal problems and difficulties are most likely to arise. It is not true to say that at such periods in the post-epileptic phase the patient necessarily indulges in automatic actions. He may do, but equally he may perform integrated, purposive, lustful actions, though such actions have a rather crude, primitive quality neglectful of all consequences.

A sergeant belonging to a crack regiment in the 8th Army was known to have suffered from a head injury for which ample radiological evidence of a fractured skull and clinical evidence of epileptiform convulsions existed in his notes. Two years later he was playing darts in the sergeants' mess for 10s. stakes. These had all been pooled in a bowl on the table which marked the deadline from which the dart players took their stance. At the subsequent court martial evidence recorded how my patient in full view of the sergeant-major had calmly appropriated the whole of the pool, put it in his pocket, walked out of the mess, urinated over the sergeant-major's desert garden, and presently had returned to the mess, where evidence admitted that he appeared mildly confused. He was subsequently charged, found guilty, and sent to a detention prison. From this sentence I rescued him by chance when I found myself sitting on a review tribunal three months later. Under ether the whole of this episode was recovered as far as the point where he got hold of his dart; then he began to twitch at the mouth and, jactitating, roused himself from the couch and proceeded to urinate in my clinic. The urination was, of course, the "automatic" or, if you will, the primitive physiological response. For this no court martial would have found him guilty. The stealing was the "non-automatic," apparently purposeful, response. At what point would the law have considered my patient responsible for his actions? There are, of course, certain moralists who might have condemned his gambling propensities, while yet others might have detected the cardinal sin of envy as the real cause of his befouling the sergeant-major's blooms.

This type of episode has very close affinities, I believe, with similar episodes which may follow quite trivial head injuries in subjects under stress. It may accompany pyrexial episodes. Most dental surgeons will have met occasional instances following local analgesia. In another part of the total clinical field these episodes are found and are related to the hysterical amnesias and the schizophrenic fugues. Occasionally they can be precipitated by a combination of these features—e.g., pyrexia with alcohol and strong emotion, or it may be a head injury.

An A.T.S. officer whom I saw in 1940 was an intrepid horsewoman known to have suffered severe head injuries some years previously. She received a t.a.b. injection on her birthday; that night she had a celebration party, went to the theatre, returned to her quarters, and at about 12 midnight (it being midsummer), phantasied that her friend was sitting on the open windowsill

beckoning her out on to the cool lawn. She walked through her first-story window and sustained a fractured spine. Was she responsible for her behaviour? I suggest it would be utter nonsense to say that she was.

Suppose such a subject, prior to the fit, head injury, fever, or other precipitating factor, subconsciously or for that matter consciously entertains lustful notions of theft, sexual assault, or aggressive intention and being in the vicinity of, or having the opportunity of performing, his phantasied action sustains a fit or becomes pyrexial, then, if such a person is on a lower cultural and possibly (but by no means necessarily) lower intellectual status, he may proceed to commit a crime and indulge his phantasy. On the contrary such a person during a period of altered consciousness may behave under certain conditions in a primitive, amoral, and savage manner. If one were asked in the Courts whether such a person would have done it "had a policeman been standing by" the answer is probably "no," but by no means necessarily no, as is shown by the following example:

A young man attending a betrothal party is overcome because he has last-minute worries concerning the wisdom of his contract as well as by the general social setting of the occasion, and drinks a little unwisely. During the supper interval his fiancée and her relatives notice that he looks pale and suggest that he goes out of the dance hall into the fresh air. Four hours later he "comes to" in a police cell with a complete amnesia of the intervening four hours. In fact he had walked up the main street of his town, and at a street corner opposite which two policemen were on duty and fully observing what was occurring he stood by a tram stop as if to await a tram to take him back to the centre of the town. An elderly woman joined him on the tram stop (which was underneath an arc light) and suddenly he attacked her, to the astonishment of the onlooking policemen, who, of course, arrested him and placed him in prison. Was this an automatic episode? The truth seems to be that our vocabulary falls to pieces whenever we attempt to describe the finesse of such an episode.

It seems to me, Sir, that the lawyers' quandary is how to define that entity upon which they seek the opinion of the physician, who in turn is foisted with the difficulty also of defining an entity which he can measure. For what is the "it" which we hold responsible at law for a person's actions, and by what test can we satisfy ourselves that this "it" is wholly integrated and acting in a unitary sense? Is it a "mind" or is it a "self"? Zeno was a clever fellow.—I am, etc.,

St. Albans. HAROLD PALMER.

The Writings of Sir Almroth Wright

SIR,—Professor Charles Singer, in his review (November 22, p. 1147) of my bibliography, "suspects" that my compilation was not a complete one—because, as he says, Wright lived to 80 and he "wrote quickly and easily, and he obviously enjoyed writing." May I correct these impressions?

I did intend my bibliography to be complete, and, so far as I know, it was to all intents and purposes. I omitted one paper—a report on vaccine therapy to a homoeopathic journal which has long since ceased to appear and which I failed to find in the chief medical libraries. I also omitted the few papers (or rather I included them only once) which were published in more than one journal; and I omitted a French translation of one English paper on wound infections.

It is a mistake to suppose that Wright wrote quickly and easily. On the contrary he frequently groaned in spirit over the labour of it. On one occasion his long-suffering secretary confessed to me somewhat sadly that he had typed one passage no less than 60 times. And Wright himself once calculated that each page of his *Prolegomena to the Logic Which Searches for Truth* had cost him 120 hours' work.

Finally, if I may disagree with Professor Singer once more on a small point, I do not think Wright himself would have wished me to omit any of his earlier papers. It was one of the sorrows of his old age that the medical profession (as he thought) had paid so little attention to them. For the most part, he did not think that the doctrine he had tried to expound was a mistaken one.—I am, etc.,

Farnham Royal, Bucks. LEONARD COLEBROOK.

POINTS FROM LETTERS

Herpes Zoster Varicellosus

Dr. L. A. GESS (Kuwait) writes: With reference to the interesting article on herpes zoster varicellosus (March 8, p. 520) I should like to submit the following case history. The patient was a European ship's captain, aged 64, without previous history of either herpes zoster or varicella, and in good health. His ship left London on March 22, calling at Port Said on April 1, where he did not go ashore, and arrived in Kuwait on April 11. He cannot recall having been in contact with any illness, but on April 6 complained of general malaise, discomfort in the chest, anorexia, and headache. The next day a generalized herpes zoster appeared along the distribution of the fifth, sixth, and seventh right thoracic nerves. On April 11, just prior to docking in Kuwait, a generalized varicellosus appeared and the patient was admitted to hospital immediately on arrival. The varicella went through the usual stages of crusting and separation and was clear by April 30, leaving minimal scars, but the herpes zoster did not heal until May 9 and even then there was residual pain and considerable scarring. No case of herpes zoster or varicella was reported from the crew of his ship or from any contacts, and the original infection was considered to have been contracted in London prior to sailing, giving a minimal incubation period for the herpes zoster of 15 days and for the varicella of 20 days.

Asthma in Childhood

Colonel F. T. HARRINGTON (Hong Kong) writes: Among a number of *Journals* which have now caught up with me is one dated September 20 containing an article (p. 636) by Dr. C. B. S. Fuller which is a survey of the work of an asthma clinic in Hampshire. It appears to me that the work done on asthma between the first and second world wars has been lost or forgotten. During that period a great deal of excellent work was done and we had sufficient knowledge of the subject to allow of cases of asthma being treated with a fair chance of "cure" and an almost certain chance of permitting the patient to live a reasonably comfortable life. . . . One mentions among others the work of James Adam, of Glasgow, Coke, John Freeman, McDowell, Storm van Lewen, Haseltine, and La Forge. All were keen and enthusiastic workers in this field, and I would suggest a study of their writings to any who intend to take up this work. For this purpose I particularly recommend the various books of James Adam, with whom I worked for a number of years on asthma. Also during that period we had the first International Asthma Congress, which was held at Mont Dore in the Auvergne. About five of us represented England, and some excellent papers were read covering the subject from a great variety of angles. These papers were published in book form and might be read with advantage. . . . The purpose of this letter is not to criticize so much as to bring to the notice of those who are working, or intend to work, in this field the work which has already been done and provide for them a taking-off point from which to continue their own line of investigations.

Pregnancy Following Immediately After Acute Pyosalpinx

Dr. MABEL F. POTTER (Bristol, 8) writes: The following case report is interesting and unusual. A woman aged 36, a multipara with four previous pregnancies, was admitted to hospital on January 4, 1952, with acute abdominal pain which was thought to be an ectopic pregnancy. A curettage was negative, but aspiration of the pouch of Douglas produced some blood-stained fluid. On opening the abdomen a double pyosalpinx with widespread acute inflammation was found. No surgical treatment was undertaken and the patient was given penicillin, 500,000 units twice a day for three days, and sulphatriad. Recovery was uninterrupted and 24 hours after operation she was transferred to a small local hospital because she wished to continue breast-feeding her 4-months-old baby. Towards the end of May when seen in outpatients she appeared to be 16–18 weeks pregnant. She was seen again in October, when she was in good general health and her pregnancy appeared to be nearly full-term.

"Et all., etcc."

Professor J. W. HOWIE (Glasgow) writes: Mr. A. L. Bacharach's support (November 15, p. 1103) for my conclusion is welcome, but the grammatical reasons for his disappointment with my analogy are obscure, especially as it survives the functional test which Mr. Bacharach applies to it. This leads him to conclude: "There can thus be no need for doubling the c any more than for doubling the l of '*et al.*' . . ." This is exactly what I thought and why I used the analogy.

Obituary

F. H. JACOB, M.D., F.R.C.P.

Dr. F. H. Jacob, for many years a consulting physician in Nottingham, died at his home at Malvern on November 25, a few weeks after his 80th birthday.

Frank Harwood Jacob was born on October 4, 1872, the son of a Naval chaplain, and received his early education at King's School, Ely. He gained the Warneford entrance scholarship to King's College, London, and thereafter he won a remarkable series of scholarships and prizes during his preclinical and clinical studies. He qualified M.R.C.S., L.R.C.P. in 1895, and, after holding the posts of house-physician and house-surgeon at King's College Hospital, became house-physician to the Nottingham General Hospital. He graduated M.B. in 1898 and proceeded M.D. three years later. In 1903 he took the M.R.C.P., becoming a Fellow in 1921. When the honorary staff of the Nottingham General Hospital was expanded in 1901 Dr. Jacob became the first assistant physician. Four years later he was promoted to the full staff, and he continued to serve the hospital faithfully until his retirement, on reaching the age limit, in 1937. In 1947, in recognition of his wonderful service to the hospital, a medical ward, the newest in the hospital, was named after him. Soon after his first appointment to the honorary staff he began to build up a large consulting practice covering Nottinghamshire, Lincolnshire, Rutland, Derbyshire, and parts of Leicestershire.

A member of the British Medical Association for over 50 years, Dr. Jacob was elected as the representative of his Division to attend the first Annual Representative Meeting of the Association, which was held at Swansea in 1903, but had, for some reason now unknown, to send a letter of apology for his absence. In 1905 he acted as one of the honorary secretaries of the Section of Medicine at the Annual Meeting at Leicester, and he was president of the Section of Medicine at the Nottingham Meeting in 1926, serving also on the Arrangements Committee in that session. He was a staunch supporter of the Nottingham Medico-Chirurgical Society and was twice elected its president, probably a unique happening in the long history of the society. He was unmarried.

Dr. P. H. O'Donovan writes : To the sick Dr. Jacob was always kind and courteous. Perhaps a reason for his great success as a consultant was his effortless ability to inspire the complete confidence of both patient and practitioner. The frequency with which patients in all walks of life volunteered their absolute confidence in him was noteworthy. As a consultant he was the best type of general physician—always punctual, never hurried, remarkably accurate in diagnosis, endeavouring always to cement the confidence between patient and practitioner ; and, finally, giving advice, erudite or sensible, as the case needed. No wonder that in a public speech some years ago a surgical colleague said that no one in the East Midlands considered it correct to die without first seeing Dr. Jacob. He had a great sense of the high ideals of his profession and by example inspired his younger colleagues. On the fly-leaf of a book he gave to me he wrote: "To love sick folk and to love helping them, to give a friendly welcome to our fellow travellers on the road of life—these are the ideals for all who work in and for hospitals."

Many of his juniors have had great cause to be thankful for kindly counsel, given always with a paternal smile of encouragement. It is not to be wondered at that he was affectionately known as "Uncle Frank." The mere accumulation of money meant nothing to him—in secret he was exceedingly generous, and probably never refused a request for help, not seldom himself paying for the treatment of a patient seen in consultation. In private life he was a man of simple tastes, taking little interest in food and drink, and, although fastidiously clean, was quite indifferent to the age of his clothes. He was fond of good music, and especially fond of the countryside, particularly Derbyshire : to him no music was lovelier than the wild whistle of the curlew or the low sweet song of the dipper.

When the last war came Dr. Jacob helped the local practitioners at Malvern, where only a short time before he had gone to live in retirement, by taking on the work of men absent in the Forces. During his retirement, too, he wrote *A History of the General Hospital near Nottingham*, which was published in 1951, a book of over 350 pages which entailed much work to a person no longer living in the locality. The hospital was founded in 1778 by John Key, a Yorkshire squire. It was written of this gentleman by his nephew: "A man who was possessed of every virtue that signifies human nature, and where generosity and benevolence were always made to the distressed." In turn this would seem a fitting epitaph for the great and lovable personality that was Dr. Frank Jacob.

J. W. S. writes : By the death of Dr. Frank H. Jacob, a distinguished and very lovable personality of Nottinghamshire has passed away. He preceded me as house-physician at the General Hospital, and we were close colleagues for nearly 40 years. On starting practice in 1901, he was given a slender bread-and-butter job by the Nottingham Health Committee to undertake routine bacteriology. Up till that time nearly all pathological material, from both the city and the hospital, had been sent to London for investigation. His laboratory, thus opened, developed, still under his guidance, to become a full pathological service for the hospital, the county, and the East Midlands, being finally taken over by the hospital about 1920. He had also had installed the first private *x*-ray plant in Nottingham, and this also developed into a service supplying the needs of practitioners in the city and county, which he continued until after the first world war. All this is evidence of the profound influence he wielded in medical developments in the district, and in many other ways he was responsible for improvements, nowhere more than in planning for the betterment of conditions at the hospital, his main objective and consideration always being the good of the patient. He was possessed of a tenacity of purpose and capacity for unremitting work without which his many and varied projects could not have materialized. His *History of the General Hospital near Nottingham*, written in a philosophic strain, and interspersed with descriptions of contemporary advances in medical knowledge and practice, makes delightful reading, and shows from the references the deep and abiding stimulus he derived from the life and works of Louis Pasteur. Jacob had a first-class brain, and, as was to be expected, became a most able, wise, and trusted physician. Although not attracted by social functions, he was a fluent and attractive speaker and could grace the big occasion, for which he was much in demand. He was as indifferent to material advantage and worldly honours as he was to the cut and style of his apparel. Cheery and friendly in nature, and himself the soul of candour, nothing aroused his indignation more than any hint of prevarication or insincerity. He was not pre-eminent in games, but in his younger days would show a tough and vigorous side in rugby football, hockey, with the gloves, or in an early morning swim in the Trent. He had deep religious convictions, without parading them, and for years had a class of young fellows on Sunday mornings, whose interest he would hold with talks on nature and science and religion. In his busiest days he would find time to take most devoted care of his mother, over 90 years of age, and during the last few years he gave himself to the nursing and care of a very severely crippled sister, resolutely refusing to leave her even for a day. So he died, looking after others to the end.

IAN E. McCRACKEN, M.D., D.P.H.

Dr. Ian E. McCracken, who was medical officer of health for Newcastle-upon-Tyne during the years 1944–5, died in London on November 30, aged 51.

Ian Earle McCracken was born on March 10, 1901, the son of a leading practitioner in Newcastle-upon-Tyne. From Oundle School he went on to study medicine at Edinburgh University, graduating M.B., Ch.B. in 1924, and proceeding M.D. in 1926. After holding resident hospital appointments in Edinburgh, he returned to Newcastle as a general practitioner. His personality and keenness brought him to the fore, but ill-health dogged him during the last part of the 14 years he spent in practice. After a series of surgical operations his health improved, and, deciding not to return to general practice, he took the D.P.H. of Durham University in 1939. His name and reputation in Newcastle then secured for him first an apppointment with the university bacteriology department and later with the Newcastle health department as assistant medical officer of health. After a few years' service he was offered and accepted, for the duration of the war, the position of medical officer of health to the city of Newcastle, which had fallen vacant when Dr. J. A. Charles (now Sir John Charles) moved to the Ministry of Health. During the years he served as M.O.H. McCracken gave courageous and unstinting service to the city, so much so that his health unfortunately again broke down, and he had reluctantly to resign. His work during this period was characterized by his personal and inspiring leadership of the staff, and by a breadth of outlook which came from long experience of the human contacts of general practice. After his health had once more improved he was appointed a lecturer in public health at the London School of Hygiene and Tropical Medicine. He was also an examiner for the D.P.H. of the Conjoint Board. Dr. McCracken's wife died nine months ago.

We are indebted to Dr. W. S. WALTON for the following appreciation: As one of McCracken's many friends who always found welcome in that sincere smile, perhaps a little grave and dignified for a moment and then almost immediately passing into the gentle geniality which reflected his warm and human personality, I regard it as a privilege to place on record a tribute to the example of sterling character and integrity which he gave to others. His room at the London School of Hygiene naturally became a calling-post for his friends who went up to London, and many would try to find some excuse to visit the School for the purpose of seeing him for a few moments. The news of his death was a great shock to his friends in Newcastle, and especially to members of the health department, where he was always welcome. It is hard to believe that no more will he put his head around the door on a surprise visit and that no more will he browse among the old records of the health department or of the University.

To me, McCracken's personality was outstanding. His influence was due to his amazing understanding of human nature. He had the rare gift of being able to project himself into other persons' shoes and to be interested in their problems and not his own. His maturity in assessment and critical judgment made him first-rate company in any discussion. It is indeed a great tragedy for the public health world that his gifts for historical research are no longer available. The three main professional phases of Ian McCracken's life—general practice in Newcastle, public health work in Newcastle, and university work in London—attracted to him many friends. They will all miss him, but they have been, and are, the richer for the privilege which was granted to them of friendship with a delightful and sincere fellow man.

H. S. MEADE, M.Ch., F.R.C.S.I.

Dr. PETER KERLEY writes: There are in Great Britain many hundreds of old students of Professor Harry Meade who like myself mourn the passing of a great teacher and a good friend (see *Journal* of November 22, p. 1155). His cool, logical outlook and his insistence on the necessity for accurate observation were an admirable foil to the spectacular and often intuitive brilliance of his senior colleague McArdle. To have walked the wards under these two was an education in itself. Harry Meade was not only a superb anatomist and surgeon but a wise counsellor and inspiring example to those who served under him. I was his dresser and later his house-surgeon during the Irish civil war. Throughout this difficult period he was a tower of strength to all around him. He never deviated from the highest principles of medicine, and for him there was neither friend nor foe, only suffering mankind. Truth did not reveal itself to him with many faces—he knew only one truth, and was quite incapable of compromise when a principle was involved. Because of this some thought him intolerant, but we who worked under him will remember him most for his tolerance of our failings and his kindly guidance in our difficulties.

We record with regret the death at Glasgow on November 10 of Dr. ALEXANDER DINGWALL, at the age of 85. Although he had retired from active practice about two years ago many of his old patients would have no other physician, and until a few weeks before his death he still was the trusted adviser to many who sought his counsel. A son of the manse, he was born in Renton, Vale of Leven, but at an early age the family removed to the North, at first to Dunbeath and later to Aultbea. From these early associations arose a deep-seated love of the Highlands and the language of the Gael. He graduated in arts at Glasgow University in 1890 and in medicine in 1893. Thereafter he commenced practice in Renton, but after a few years returned to Glasgow, where his genial disposition soon won him many friends and a large private practice. He was one of the old school of practitioners to whom monetary reward meant little, and there were few West Highlanders in Glasgow who did not at some time or other have reason to call him blessed. He was closely associated with all Highland societies, and seldom was he an absentee from the Mod, where he was a handsome and distinguished figure invariably attired in full Highland dress. He was a past president of the Caledonia Medical Society, of the Rossshire Benevolent Association, and of the Glasgow University 93 Club, which included among its members men distinguished in the Church, in Medicine, and in Law. Although well over military age, he served with the R.A.M.C. from 1915 to 1918. On demobilization he was appointed to the Ministry of Pensions staff in London, where he worked for three years, but life as a Civil Servant had little attraction for one of his temperament, and in 1921 he returned to practice in Glasgow, where he quickly regained a leading place in the medical life of that city. He did not accept service under the N.H.I., for he was essentially an individualist, and preferred the more personal and satisfying links that are found in private practice. In 1924, when regional offices were instituted by the Department of Health, he was appointed as the first part-time referee in Scotland, an office to which he gave invaluable service until after his 80th birthday. On the outbreak of war in 1939 he gave his services to military recruiting boards, where young and old found in him an efficient and kindly colleague. He was keenly interested in all facets of medicine, but essentially he was the beloved and trusted physician, endeared to both patients and colleagues alike. He spoke no evil, nor listened to it, and often he would say, "If you can't speak well of him, keep silent." The attendance at the funeral service was large and representative of all branches of medicine and commerce in the city, and also included many who had made the long journey from the Highlands to pay their last tribute to one whose personality will long be remembered

in the North. Of him, as of Mr. Greatheart, it can be said, "When he passed over, all the trumpets sounded for him." —I. D. G.

Dr. ROBERT PORTEOUS, who died suddenly in Edinburgh on November 6 at the age of 57, was a doctor of unusual experience and distinction. He was born at Pumpherston, Midlothian, and educated at Broxburn High School. Early in life he determined to be a doctor, but family circumstances made necessary another choice of career. He therefore studied engineering at the Heriot Watt College, Edinburgh, where he distinguished himself as a student. During the 1914–18 war he was employed in the Western Aircraft Company, and in 1921 qualified as A.M.I.Mech.E. Still determined to be a doctor, he went to the U.S.A. in 1926, prepared to tackle any job, and he returned to this country 15 months later, having earned and saved enough money to pay for five years of study at Edinburgh University. There he again showed himself a student of distinction, being Vans Dunlop Scholar in materia medica and medicine, a gold medallist, and gaining first prize in clinical surgery. He graduated M.B., Ch.B. in 1932, and for two years was assistant medical officer at Bradford City Sanatorium, where he designed a universal splint for the treatment of bone and joint tuberculosis, a description of which he published in 1934. Proceeding M.D. in that year, he built up during the next 17 years a large and successful general practice in Blackburn, Lancashire. In 1941 he was appointed honorary physician to Blackburn Royal Infirmary, and in 1945 honorary physician to Queen's Park Hospital. Last year family circumstances compelled him to leave his practice and hospital and return to Edinburgh, where he entered the school health service. He addressed himself to this new work with zeal and had already distinguished himself by his interest in its many problems, especially in the prevention of postural defects and in health education. To a wide knowledge of medicine Dr. Porteous added the lessons of his earlier experience as an engineer. Forthright honesty, energy, common sense, and friendliness were among his characteristics. Home life and his profession absorbed most of his interest, but he found time for golf and gardening, and he played a good game of snooker. He was a very lovable man. Former colleagues, nurses, and patients will deeply mourn his loss; so will the teachers and children in the schools where he spent the last very happy year of his life. Our sympathy goes out to his wife, the companion of his outstandingly happy married life.—W. N. B. W.

Medical Notes in Parliament

Collection of Vital Statistics

On December 2 the House of Commons went into committee on the Expiring Laws Continuance Bill. When the schedule was considered Mr. EDWARD SHORT moved to leave out the section relating to the Population (Statistics) Act, 1938. He said the Act was so important that it should not be included in the Bill but enacted separately as a permanent measure. The Act made provision for obtaining statistical information about the population of Great Britain. The information was to be collected from the registration of births, stillbirths, and deaths, and the duty of collecting was laid on the Registrar-General, who must comply with directions given to him by the Minister of Health. It was ridiculous that the Bill under which these statistics were collected should have to be renewed from year to year. Adequate and reliable statistics were essential in planning the Welfare State, as National Insurance benefits had to be equated with contributions, and such calculations could only be made on accurate statistics.

Mr. S. T. SWINGLER said that a 10-year limit had been imposed in the original statute, which therefore expired in 1948 but had been renewed year after year. The Government should produce a Bill along the lines of the measure of 1938 and make it part of the permanent legislation.

Mr. W. Ross said that when the Bill was introduced in 1938 Sir Kingsley Wood had to face terrific opposition, but the system had now been accepted by the public and was seen to be of service to the nation. The information asked for in 1938 had been suggested in the report of the Registrar-General in 1867 as necessary in considering population policy. From 1867 to 1938 nothing was done until someone discovered that the Scots had done it about 70 years before. In 1947 the Royal Commission on Population discovered that the statistics given to them for examining the problem were inadequate and they had to ask the Government of the day for a special sample census of the population to be taken.

Mr. A. BLENKINSOP said it would be helpful if an indication were given as to whether any objection had been taken over the years to the provision of this information.

Miss P. HORNSBY-SMITH replied. She said that if the amendment were pressed it would deprive the Registrar-General of what all agree were vital and important statistics. The Government hoped to be able eventually to find Parliamentary time to put the matter into a permanent form. Other considerations must weigh in the framing of new permanent legislation. The Act as continued under the Expiring Laws Continuance Act enabled the country to provide statistics far more comprehensive than those furnished by most other countries. Without the continuance of the 1938 Act the Government could not provide comprehensive information for the World Health Organization. It would not be so well informed in anticipating future problems, such as the numbers of nurses and midwives it would require. There was valid reason for allowing another short span of time so that the Government could make full use of final reports under the census and under the report of the Royal Commission on Population.

Mr. SHORT then withdrew his amendment.

Smaller Waiting-list

Replying on December 4 to Mr. A. EDWARD DAVIES, Mr. IAIN MACLEOD stated that returns submitted annually by hospitals showed that during 1951 the waiting-list dropped by nearly 27,000 and the average daily number of occupied beds increased by over 4,000. A very small reduction in the average length of stay of patients or in the proportion of beds unoccupied would make a considerable difference to waiting-lists. The Ministry of Health was discussing with the regional hospital boards how improvements on these lines could best be achieved.

Anthrax Vaccine for Livestock

Sir THOMAS DUGDALE announced on December 4 that research work had resulted in the production of satisfactory vaccine for the protection of livestock from anthrax. This vaccine was being made available to veterinary surgeons. Inquiries into sources of infection and possible further safeguards were in progress.

Numbers of Prescriptions Compared

Replying on December 4 to Mr. A. BLENKINSOP, Mr. IAIN MACLEOD furnished the following statistics for England and Wales showing that the number of prescriptions in October, 1952, was 18,662,000, compared with 20,358,621 in October, 1951. The numbers of surgical appliances delivered to hospitals in October, 1952, with the figures for October, 1951, in parentheses, were as follows: surgical footwear (pairs), 3,955 (3,534); surgical abdominal appliances, 5,996 (8,319); elastic hosiery (orders—pairs or single), 3,242 (3,054); wigs, 593 (938).

Cortisone and A.C.T.H.

Answering Mr. KENNETH ROBINSON on December 4, Mr. IAIN MACLEOD replied that during the time that cortisone and A.C.T.H. had been under trial in this country much valuable information had accumulated as to their

uses and limitations, but their place in the treatment of rheumatoid arthritis and allied conditions was not yet definitely determined. A decision as to the possible extension of their distribution would be made as soon as possible. There was some British production of cortisone and A.C.T.H. The F.O.B. value of Government imports of cortisone during the 12 months ending October 31, 1952, was £105,000, and of A.C.T.H. £111,428.

Mental Defectives.—The approximate numbers of adults certified as mentally deficient were 1,678 in 1949, 1,697 in 1950, and 1,772 in 1951. Figures for earlier years are not available.

Age of Coal-miners.—In 1951 the average age of coal-miners in the United Kingdom was 40.5 years for all wage-earners and 39.1 years for face workers.

Medico-Legal

FATAL BLOOD TRANSFUSION

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Mistakes over blood groups in transfusions are unhappily all too common. How easy and how disastrous it is to make them is illustrated by the story told before the Croydon Borough coroner on November 6 and 10 during the inquest on Mrs. Mary Kate Williams.

Mrs. Williams, a healthy woman of 21, was expecting her first baby on October 16, 1952. On October 27 she was admitted to St. Mary's Maternity Hospital, Croydon, for confinement, and after the birth of her baby Dr. A. Schutz was called to see her because the uterus would not contract and blood was trickling away. After unsuccessfully trying to express the placenta Dr. Schutz sent for Dr. T. G. E. White, the senior registrar at the Mayday Hospital, and told the nurse to get ready for a blood transfusion. Dr. White decided that a transfusion was necessary. No stock of blood is kept at St. Mary's, so the transfusion, which was very difficult to start, was initiated with "plasmosan." The nurse ordered two pint bottles of blood from the Mayday Hospital, the normal source of supply for St. Mary's. She ordered the group shown on the patient's case notes, which was O Rh-positive. When the blood arrived Dr. Schutz checked the label on the bottles with the case notes and found them correct. Transfusion was started.

Later, more blood was needed, and Dr. Schutz telephoned the Mayday Hospital for a further two pints of O Rh-positive blood. The message was passed to the labour-ward sister who had sent the two previous bottles to St. Mary's. She knew there was no more O Rh-positive blood in the maternity refrigerator, so she instructed the nurse pupil midwife on duty to collect it from the laboratory and give the bottles to the porter to take to St. Mary's. The nurse understood that she had been asked to get group A Rh-negative blood. This was obtained, and the porter took two pint bottles of A Rh-negative blood to St. Mary's.

The patient's blood pressure fell below 90 mm. Hg, and therefore according to instructions from Dr. Schutz the nurse put up a third bottle of blood. She knew that this had been specially ordered for the patient and was the only blood they had. She did not check the label against the case sheet, nor look at the bottle to see what group it was, assuming that it would be the same as the two previous bottles. When 3 or 4 oz. had gone out of this bottle, the patient suddenly collapsed and died within 20 minutes.

Dr. David Haler, who carried out the necropsy, came to the conclusion that Mrs. Williams had been gravely ill with post-partum haemorrhage associated with an unduly adherent placenta. She was undoubtedly improving under treatment, and since her final collapse followed the administration of a relatively small amount of blood of the wrong group he was forced to the conclusion that this transfusion accelerated her death. Without it she might have lived.

The coroner recorded a verdict of death by misadventure.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **November 22** (No. 47) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	41	4	13	0	1	29	2	14	0	2
Dysentery	158	29	57	0		221	45	45	6	
Encephalitis, acute	3	0	0	1		4	0	0	1	
Enteric fever:										
Typhoid	3	0	0	2	1	5	0	0	0	2
Paratyphoid	8	1	0	0		14	0	6(B)	0	
Food-poisoning	77	17		0		104	25		1	
Infective enteritis or diarrhoea under 2 years				6	18				20	13
Measles*	12,130	1129	174	24	178	2,047	22	120	143	69
Meningococcal infection	28	1	16	0	3	46	4	12	2	4
Ophthalmia neonatorum	35	2	10	0		32	2	11	0	
Pneumonia†	519	46	341	3		430	33	199	6	
Poliomyelitis, acute:										
Paralytic	62	3	6	1	2	41	2	7	2	3
Non-paralytic	21	2				16	2			
Puerperal fever§	227	36	11	3	1	243	20	20	0	1
Scarlet fever	2,226	188	370	38	83	1,476	120	335	43	50
Tuberculosis:										
Respiratory			134	31				141	30	
Non-respiratory			36	12				31	6	
Whooping-cough	1,854	108	97	36	96	1,891	62	335	52	58

DEATHS in Great Towns	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0		0	0	*0*	0	*0*	0	0
Dysentery	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0		0		*0*	0	*0*	0	
Infective enteritis or diarrhoea under 2 years	7	0	2	0	0	*13*		*1*	0	0
Influenza	11	1		0	1	*6*	0	*1*	0	1
Measles		0		0	0		0	*1*	0	0
Meningococcal infection		1					0	*1*		
Pneumonia	190	31		9	6	*156*	23		15	4
Poliomyelitis, acute	5	0			0	*4*	1			0
Scarlet fever		0		0	0		0	*0*	0	0
Tuberculosis:										
Respiratory	133	18	15	4	2	*119*	10	*16*	3	8
Non-respiratory		0	2	2	0		5	*3*	0	1
Whooping-cough	1	0		0	0	*3*	1	*0*	0	0
Deaths 0–1 year	206	18	33	10	11	*203*	31	*22*	4	9
Deaths (excluding stillbirths)	5,302	753	569	112	137	*4,530*	680	*548*	124	168
LIVE BIRTHS	6,701	955	715	207	323	*6,113*	1019	*779*	217	365
STILLBIRTHS	183	17	20			*180*	19	*16*		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

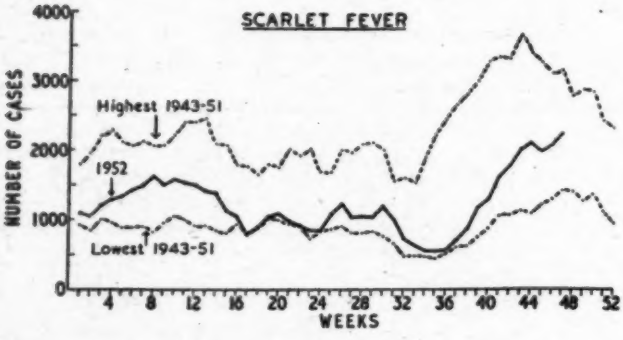
Lung Cancer and Respiratory Tuberculosis

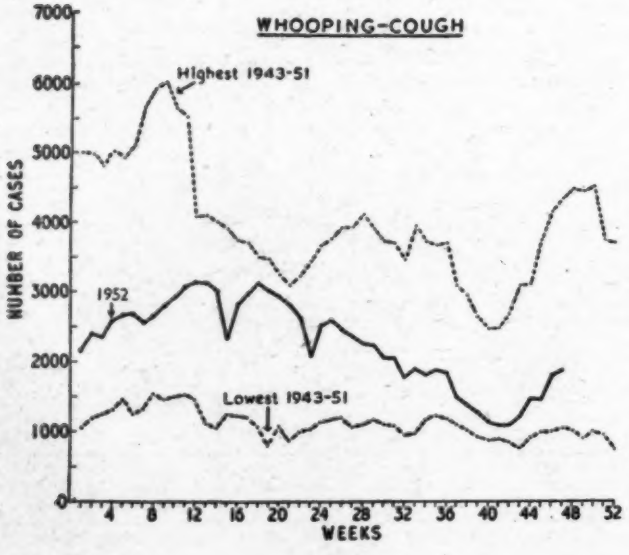
For the first time in 1951 the number of deaths from cancer of the bronchus and lung for England and Wales exceeded the number of deaths from respiratory tuberculosis. Lung cancer is the subject of an article by Dr. R. Doll and Professor A. Bradford Hill in our opening pages this week and a leading article at page 1299. A comparison of numbers of deaths in England and Wales for 1947–51 is given in the Table below, which shows how deaths from respiratory tuberculosis have declined while those from cancer of the bronchus and lung have increased in that period.

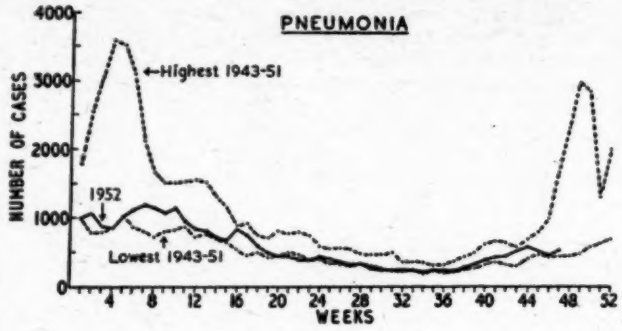
Year	Respiratory Tuberculosis	Cancer of Bronchus and Lung
1947	19,753	9,535
1948	18,798	10,463
1949	17,388	11,272
1950	14,084	12,232
1951	12,036	13,233

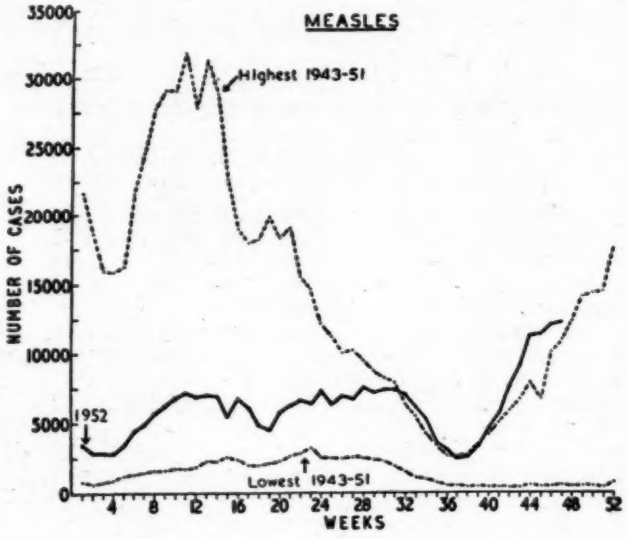
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1943–51 are shown thus - - - - - -, the figures for 1952 thus ————. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

Small rises were reported in the number of notifications of infectious diseases in England and Wales during the week ending November 22. These included 161 for scarlet fever, from 2,065 to 2,226; 95 for measles, from 12,035 to 12,130; 74 for whooping-cough, from 1,780 to 1,854; and 67 for acute pneumonia, from 452 to 519. The only decrease of any size was 53 for dysentery, from 211 to 158.

Only small variations were reported in the local trends of scarlet fever and whooping-cough. Considerable fluctuations occurred in the local trends of measles. The largest rises were 176 in Suffolk, from 208 to 386; 152 in Kent, from 600 to 752; and 133 in Nottinghamshire, from 397 to 530. The largest falls were 261 in Yorkshire West Riding, from 1,093 to 832; 185 in the Soke of Peterborough, from 302 to 117; and 102 in Durham from 550 to 448. The number of notifications of diphtheria, 41, was 3 less than in the preceding week. The only local variation of note was a fall from 6 to 1 in Staffordshire. Almost half of the cases of diphtheria were notified in three towns—Liverpool C.B. 7, Birmingham C.B. 6, and Redditch U.D. 5.

83 cases of acute poliomyelitis were notified; these were 20 fewer for paralytic and 1 fewer for non-paralytic cases than in the preceding year. The largest returns were Essex 11, Lancashire 8, and London 5.

The largest returns for dysentery were Lancashire 48 (Manchester C.B. 15, Blackpool C.B. 14, Liverpool C.B. 12), London 29 (Lewisham 7), Durham 11 (Darlington R.D. 6).

Week Ending November 29

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 2,399, whooping-cough 2,138, diphtheria 20, measles 14,791, acute poliomyelitis 77, dysentery 197, paratyphoid fever 4, and typhoid fever 1.

Medical News

Yellow Warning.—On December 9 the London Emergency Bed Service issued a yellow warning to hospitals because the percentage of admissions had fallen below the critical figure of 80% (see *Journal*, December 22, 1951, p. 1516). The number of applications made to the Service for admission to hospital during the seven days ending December 8 was 1,897, of which 79.86% were admitted.

Jubilee Dinner of the Central Midwives Board.—Under the chairmanship of Mr. Arnold Walker, the members of the Central Midwives Board and some 100 guests celebrated the 50th anniversary of the Board at a dinner in the Apothecaries' Hall on Wednesday, December 3. The Minister of Health, Mr. Iain Macleod, M.P., who was the principal guest, could make only a brief speech before returning to urgent business in the House of Commons. He referred to the admirable relationship which had always existed between the Ministry of Health and the Board in their common concern with the maternal and infant mortality rates of the country. He looked forward to even greater achievements in the future. Sir John Charles, Chief Medical Officer of the Ministry of Health, deputized for the Minister, and in proposing the health of the Board paid tribute to the work of its chairmen, but, he said, "Captains and kings cannot alone maintain an empire—particularly an empire of women." The high status of midwives to-day was, he went on to say, due to the training that they had received to fit them to accept professional responsibility. Mr. Arnold Walker, replying for the Board, regretted that the maternity service had been trichotomized by the 1946 Act. The guests were welcomed by Professor A. A. Moncrieff, vice-chairman of the Board, in a happy speech to which Sir Wilson Jameson, Master of the Society of Apothecaries, responded. The toast of the midwifery profession was proposed by Sir Allen Daley and gracefully acknowledged by Miss N. B. Deane, president of the College of Midwives.

Eightieth Birthday of Einar Key.—Professor Einar Key, a foreign corresponding member of the B.M.A., celebrates his eightieth birthday on December 14. His father, Axel Key, was professor of pathological anatomy at the Karolinska Mediko-Kirurgiska Institutet and editor of *Nordiskt Medicinskt Arkiv*, forerunner of *Acta Medica Scandinavica* and *Acta Chirurgica Scandinavica*. Einar Key has been editor of the latter since its inception in 1919, and also a distinguished practising surgeon, being professor of surgery at the Karolinska Institutet. He has made important contributions to urological and pulmonary surgery, his operative technique in embolectomy of the lower extremities being particularly notable. The Key family is of Scottish origin, for two members of the Mackay family joined the Swedish Army during the Thirty Years War and later settled in Sweden under the name of Cay or Kay, later changed to Key.

Institute of Psycho-analysis.—After Professor Roger W. Russell had delivered the fifth Ernest Jones Public Lecture at the Royal Society of Medicine on December 1, the British Psycho-analytical Society held a reception in the new premises of the Institute of Psycho-analysis at 63, New Cavendish Street. The Institute, which has not been "nationalized," was established in 1924 in a house in Gloucester Place. Two years ago the lease of the new premises was bought and the internal alterations have now been nearly completed. On the second and third floors there are at present 13 treatment rooms for adults and 3 for children. Further expansion is planned. There are 66 students attending the Institute, and the teaching staff numbers 31. The patients are chosen by the director of the clinic, and the only treatment given is psycho-analytical. At present 117 adults and 18 children are under treatment. About 25% of these are being treated under contractual arrangements made with the North-West Metropolitan Regional Hospital Board.

Everest Expedition.—The British team which goes to Everest next spring will include two, and probably three, medical men. The team's medical officer is to be Dr. M. P. Ward, who qualified from the London Hospital in 1949. In addition there will be Mr. R. C. Evans, a neurosurgical registrar at Liverpool, and probably Dr. L. G. C. Pugh, from the National Institute for Medical Research, as the expedition's physiologist. All three have been to Everest before.

Family Planning Conference in India.—The Third International Conference on Planned Parenthood has just been concluded at Bombay. It was attended by some 400 delegates coming from 14 countries, which included the United States, Great Britain, and Pakistan. The conference was the first of its kind in Asia, and was concerned particularly with the social, economic, and cultural factors which affect the growth of populations. Among the contributions to the conference were reports of surveys of the attitude of Indian mothers to family planning; one of these, from Baroda, showed a very favourable response to the idea of birth control.

Braille.—The blind and those concerned with their welfare have been celebrating this year the hundredth anniversary of the death of Louis Braille (1809–52). Braille's system of reading and writing is used by blind people throughout the world, and the output of Braille literature is now very large. Last year the National Institute for the Blind, London, the largest printing and publishing house for the blind in the Commonwealth, printed over 45,000 books, about 400,000 newspapers, and nearly 130,000 magazines. This is the most the Institute's present plant can produce, but a new printing method, the "solid dot process," which it is hoped will both cheapen and quicken production, has been tested and is now being developed for large-scale use.

Child Health in Manchester.—Dr. Catherine Chisholm, the first woman to be accepted as a medical student by Manchester University, and whose death was recorded in the *Journal* of August 2 last (p. 287), left £17,600. After a few legacies she left one-half of the residue for the promotion of research into the health and diseases of infants, to be known as "The Alice Chisholm Fund" in memory of her sister, and one-half "to the Victoria University of Manchester to be applied in or towards the endowment of the School of Child Health in or attached to that University." The university has appointed a committee to consider the application of this bequest.

Foundling Hospital Bill.—Notice was given in *The Times* last week that the "governors and guardians" of the Foundling Hospital are seeking to introduce a private Bill to make it possible for children brought up at the hospital to avail themselves of the shorter birth certificate which does not disclose parentage. At present, on the children's birth certificates the name of the Foundling Hospital appears as guardian. According to the secretary of the hospital, about 3,000 persons are affected.

New Danish Medical Periodical in English.—There is a striking disproportion between the importance of Danish contributions to medicine and the limited scope of the Danish language. To remedy this the Danish Medical Association is to commence publication in January, 1953, of the *Danish Medical Bulletin* in English. It will contain short articles and communications, abstracts, and summaries of reports on medico-social affairs. Copies will be sent free to foreign libraries, teaching hospitals, research institutes, public health authorities, and the like. Individual subscribers will be asked to pay a small fee. The *Bulletin* will appear ten times a year, with a total of 360 pages, and will be published under the direction of the editors of the *Ugeskrift for Læger*, representatives of medical faculties, etc.

Tuberculosis in New Zealand.—Already New Zealand is spending £3.5m. on the eradication of tuberculosis. One of the difficulties is the detection of cases in the remote country areas. At present all the mass radiography units are located in the large towns, but early next year the Government is providing three mobile units to deal with this problem.

Prizes for Amateur Films.—A prize of 100,000 francs (about £100) is again offered by *La Presse Médicale* for the best 16-mm. silent or talking film made by an amateur for medical or surgical teaching purposes. The prize may be divided and there will be several other awards. No film subsidized or made by a laboratory or firm will be considered. The closing date of the competition is March 10, 1953. Further particulars may be obtained from *La Presse Médicale*, 120, Boulevard St. Germain, Paris, 6e.

Reminder.—All applications for stands at the Scientific Exhibition at the 1953 B.M.A. Annual Meeting must be received at the latest by the end of this year. Application forms are obtainable from the Secretary, B.M.A. House, Tavistock Square, London, W.C.1. Further information about the exhibition will be found in the October 18 issue of the *Journal* (pp. 874 and 879).

Radioactive Substances Advisory Committee.—Sir Charles Darwin, F.R.S., formerly director of the National Physical Laboratory, has succeeded Sir Henry Dale, F.R.S., as chairman of the committee which advises the Government on the protection of both workers and the public against radioactive materials. A new medical member of the committee is Professor G. R. Cameron, F.R.S.

Medical Golfing Society.—The society's annual dinner was held at the Mayfair Hotel, London, on December 4. The guests included Lord Brabazon of Tara, Mr. Philip Gee, and Mr. Henry Longhurst. Mr. R. Lindsay-Rea was elected president and Dr. D. R. Murray captain for the coming year.

Bequests.—Mr. Henry Law Jackson, formerly a governing director of Messrs. H. K. Lewis and Co. Ltd., the medical publishers and booksellers, left the residue of his estate, after payment of certain legacies, his one-third share of freehold premises in Gower Street and Gower Place, and his freehold residence upon trust to his wife for life, and then to University College Hospital Medical School to form a scholarship or prize tenable for two years, to be known as the "Jackson Lewis Scholarship or Prize."

Rose Simmonds Memorial Fund.—The British Dietetic Association is opening a fund in memory of Miss Rose Simmonds, the first trained dietitian in this country and a pioneer in her subject, who died last year. The fund will be used to provide prizes or scholarships in dietetics. Donations to the fund are invited, and should be sent to the treasurer of the British Dietetic Association, 251, Brompton Road, London, S.W.3.

Dr. E. W. L. Thompson has been appointed Master of the Rotunda Hospital, Dublin, in succession to the late Professor O'Donel Browne. Dr. Thompson was previously Assistant Master.

COMING EVENTS

Health Education at School.—The Ling Physical Education Association will hold a three-day course in "Health Education in the Secondary School" at the Victoria Hall, London, W.C.1, from January 5 to 7, 1953. The opening address will be given by Sir John Charles, and there will be talks and practical demonstrations on various aspects of the subject. Further details may be obtained from the secretary of the association, Hamilton House, Bidborough Street, London, W.C.1

International Congress of Microbiology.—The Sixth International Congress of Microbiology will be held in Rome from September 6 to 12, 1953. Further information may be obtained from the following address: VI Congresso Internazionale di Microbiologia, Istituto d'Igiene (G. Sanarelli), Città Universitaria, Roma.

SOCIETIES AND LECTURES

Details in this column are necessarily brief. Further information and tickets where required (marked ●) should be obtained from the institution concerned.

Saturday, December 13

SOUTH-EAST REGIONAL TUBERCULOSIS SOCIETY.—At Kings College Hospital Medical School, S.E., 10.30 for 11 a.m., Dr. J. L. Livingstone: Eosinophilia of the Lung

Monday, December 15

●INSTITUTE OF CHILD HEALTH.—5.30 p.m., Professor E. C. Amoroso: Comparative Physiology.

ROYAL EYE HOSPITAL.—5 p.m., Dr. T. H. Whittington: Myopia, and the Care and Treatment of the Myopic Patient.

Tuesday, December 16

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5 30 p.m., Professor J. D. Boyd: Development of the Heart in Relation to Congenital Heart Disease.

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 8.30 p.m., discussion to be opened by Mr. Basil Q. Henriques and Dr. W. Moodie: Juvenile Delinquency.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. B. Dowling: Tuberculosis of the Skin.

SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, S.W., 8.30 p.m., Mr. R. U. Gillan: Some Common Symptoms Referable to the Eye and Their Significance.

WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Dr. Douglas Gordon: When the Electroencephalogram Helps.

Wednesday, December 17

CAERNARVONSHIRE AND ANGLESEY PAEDIATRIC CLUB.—At Clinic, Sackville Road, Bangor, 4.30 p.m., Mr. R. P. Osborne: Plastic Surgery in Children.

FELLOWSHIP FOR FREEDOM IN MEDICINE, LTD.—At Reynold's Restaurant, Wolverhampton, 7.45 for 8 p.m., dinner; 9 p.m., discussion.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. C. D. Calnan: Treatment of Fungus Infections.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Arnott Demonstration by Professor R. J. Last: The Pectoral Girdle.

Thursday, December 18

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor A. Hemingway: Dynamics of the Heart Beat

EDINBURGH CLINICAL CLUB.—At B.M.A. Scottish House, 8 p.m., Mr. T. I. Wilson: Urology as Seen by the General Practitioner.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 8.30 p.m., Films: (1) Radiography of the Vertebrae; (2) Carcinoma of the Rectum; (3) Pyloric Stenosis.

Friday, December 19

BIOCHEMICAL SOCIETY.—At Medical College, St. Bartholomew's Hospital, Charterhouse, E.C., 2 p.m., scientific papers.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. G. B. Dowling: Tuberculosis of the Skin.

ROYAL EYE HOSPITAL.—5.30 p.m., Mr. Howard Reed: Slit-lamp Appearances and their Diagnostic Value.

APPOINTMENTS

BRODIE, ANDREW SINCLAIR, M.B., Ch.B., D.P.H., County Medical Officer of Health and Group Hospitals Officer for Orkney.

ELLIS, MAURICE, M.B., B.Chir., F.R.C.S., D.T.M.&H., Consultant Surgeon in Charge of Casualty Department, General Infirmary at Leeds.

MARTIN, KENNETH W., M.S., F.R.C.S., Resident Assistant Surgeon, St. Thomas's Hospital, London, S.E.

WARREN, M. D., M.D., D.P.H., D.I.H., Deputy Medical Officer of Health for Hampstead and Assistant Medical Officer, London County Council.

WILSON, HENRY DONALD, M.B., Ch.B., D.P.H., D.I.H., County Medical Officer, East Lothian.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bullough.—On December 1, 1952, at Hope Hospital, Salford, Lancs, to Anna, wife of A. S. Bullough, M.B., F.R.C.S., a daughter—Irma.

Collinson.—On December 2, 1952, at Rotherham Nursing Home, Yorks, to Desne (formerly Service), wife of Dr. Peter Collinson, of Cortworth Cottage, Wentworth, Yorks, a son.

Divers.—On November 30, 1952, to Betty (formerly Craig), wife of Dr. Lloyd Divers, of York Lodge, Horley, Surrey, a son.

Fraser.—On November 16, 1952, to Mary (formerly Chalmers), M.B., Ch.B., wife of Robert J. A. Fraser, F.R.C.S.Ed., 77, Anderson Drive, Aberdeen, a daughter.

Wilkinson.—On December 6, 1952, at St. George's Hospital, Wallingford, Berks, to Sheila, wife of Dr. O. C. Wilkinson, of The Willows, Cholsey, Berks, twins—a son and a daughter.

Wilmot.—On November 29, 1952, at Tyrone County Hospital, Omagh, Northern Ireland, to Patricia (formerly Harmsworth), wife of Mr. T. J. Wilmot, M.S., F.R.C.S., a son.

MARRIAGES

Rowe—Cowling.—On November 5, 1952, at Exeter, Alan Inness Rowe, M.B., B.S., to Sheila Nancy Cowling, S.R.N.

DEATHS

Clyne.—On November 18, 1952, at his home, London, S.W., James Wilson Clyne, M.B., Ch.B.

Johnson.—On November 17, 1952, at Bridge House, Gainsborough, Lincs, George William Johnson, M.B., B.Ch.

Johnson.—On November 20, 1952, at the Tavistock Hospital, Devon, Benjamin Johnson, D.S.O., M.B., B.Ch., Colonel, late R.A.M.C., retired, aged 69.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

The Pregnant Radiotherapist

Q.—*Should a radiotherapist continue at her work when she becomes pregnant?*

A.—There would appear to be no reason for advising a woman who has become pregnant to give up her work as a radiotherapist. It is of course assumed that adequate measures for the protection of staff exist (see *Recommendations of the British X-ray and Radium Protection Committee* (7th Revised Report), October, 1948). Provided the tolerance dose of irradiation is not exceeded, there is no reason to suppose that the foetus will suffer any ill-effects.

From the purely practical point of view the developing ovum is most susceptible to damage of any sort in the first few weeks following fertilization, and any theoretical radiation effect would have already occurred by the time pregnancy was definitely established.

Magnifying Power of Microscopes

Q.—*What sets the limit on the magnifying power of the different kinds of microscope? Please indicate the theoretical and practical limits for the different varieties.*

A.—The theoretical limit of the resolution is set by the wavelength of the light used, and is one-third to one-half of it. For example, white light has a mean wavelength of approximately 500 m.μ, and therefore a light microscope of maximum power is unable to distinguish as separate entities two particles which are less than 200 m.μ apart. Stated in another way, it cannot be expected to reveal a virus particle 200 m.μ in diameter. About half this resolution is obtained in practice with oil-immersion objectives. By using ultra-violet light of mean wavelengths 250 m.μ the quartz microscope has a theoretical limiting resolution of 100 m.μ and a practical one of about 300 m.μ.

The equivalent wavelength of electrons depends on their energy. If they are accelerated by a potential of 50,000 volts, the equivalent wavelength is only 0.005 m.μ. The extremely high resolution which this implies is never obtained in the electron microscope, but objects have been discerned as small as 5 m.μ. They are, of course, more difficult to see if they consist of material of low contrast, as do all biological objects.

Treatment of Sycosis Barbae

Q.—*What treatment is advised for a case of sycosis barbae of nine months' duration? Only partial control has been achieved by local and systemic chloramphenicol, and in view of possible toxic side-effects I am not keen to pursue this line of treatment for too long.*

A.—One or other of the antibiotics will usually give better results than the older treatments; however, the application of a hydroxyquinoline preparation ("vioform" cream or "quinolor" ointment) should still be tried if the antibiotics do not seem to be effective. The most recent clinical trials have suggested that the best results are to be obtained with 1% terramycin cream. In recent years attention has been drawn to the importance of staphylococcal carriers in perpetuating sycosis barbae and in causing relapses. The sites of carriage are most often the anterior nares and sometimes the conjunctival sac. Infected gums and the upper respiratory tract, including sinuses and antra, should be most carefully examined from this aspect.

Night Starts

Q.—*A man in his sixties complains that every night, just as he is dropping off to sleep, he suddenly starts up in a state of anxiety or is wakened by sudden jerks of his legs. What are the causes of these symptoms, and what treatment is advised?*

A.—The night start, or sudden muscular jerk occurring just on the point of dropping off to sleep, has been experienced by most people, and in some is of such frequent occurrence as to be vexatious. The causation is unknown, but is probably connected with a less than absolutely even spread of inhibition in the nervous system in the process of going to sleep, so that some centres maintain activity, even of a disorderly kind, to a later stage than usual, or, perhaps, show a form of release after higher controlling centres are inhibited. Phenomena of a similar kind are shown in the sensory field in the form of hypnogogic hallucinations.

It is unusual for night starts to be made the subject of complaint to a doctor. When that occurs, it is usually because the patient is over-sensitive and over-anxious and is worrying about them when he need not. In that case reassurance will do much to put things right, unless the patient is so anxious that he does in fact need general treatment for an anxiety state. The facts communicated as a basis for the question suggest that this last possibility is the case. It is unlikely that the patient suffers from anxiety only at night, and he probably has similar symptoms during the day, though he may then be better able to cope with them. This would indicate the need to examine his circumstances for causes of worry and anxiety and to find ways of obviating them if possible. Purely as symptomatic treatment one might suggest the use of a small dose of a rapidly acting barbiturate, such as amylobarbitone or quinalbarbitone sodium, to shorten the process of dropping off to sleep and to allay anxiety during it.

Mixing Insulins

Q.—*Is there any objection to mixing different kinds of insulin—e.g., soluble and P.Z.—in the same syringe so that a single injection may be given instead of two?*

A.—It is quite usual for soluble and protamine-zinc insulin to be given together in the same syringe as a mixed injection. If this is done the soluble insulin should be introduced first into the syringe and then the P.Z.I. It should be remembered, however, that if this is done a small amount of the soluble insulin will be converted into P.Z.I. owing to the excess of protamine in the latter preparation.

Irregular Menstruation and Fertility

Q.—*A woman of 26 with a very irregular menstrual history is now contemplating marriage, and wants to know whether she is likely to be infertile or not. How may I reach a reliable prognosis? Her periods started at the age of 15 and were then regular (7/28) but heavy, amounting to flooding at times. After a year of this the periods became very infrequent (once or twice a year), lasting about four days and moderate in amount, usually occurring during her holidays. They continued thus for the next 10 years. Since December, 1951, she has been doing a little courting, and in January she had a normal period; since then she has menstruated every three weeks. Her secondary sexual characters are normally developed.*

A.—The most certain method of assessing this woman's fertility would be to carry out a full investigation including examination under anaesthetic, tubal patency tests, endometrial biopsy, and possibly daily records of the basal temperature. But it is extremely doubtful whether it is justifiable to do this provided her general health is good and the pelvic organs feel normal on examination. The evidence given suggests that she is an individual whose ovarian and uterine cycles are essentially normal but are easily temporarily disturbed by all manner of emotional

and environmental factors. This is not uncommon and is usually of no significance. Judging by what has happened since her engagement it is quite likely that marriage will have a good effect in regulating the cycle. In any case, however, fertility is not likely to be seriously affected.

The Bed-bug

Q.—*For what diseases may the bed-bug be responsible? What is the best way of disinfecting a hospital ward, where cracks in the floors and skirting appear heavily infested? What are the chances of reinfestation by bed-bugs brought in by patients?*

A.—The bed-bug is not responsible for the transmission of any diseases.

It is nowadays an easy matter to exterminate bugs from floors or other structures. All cracks, etc., should be sprayed with a 5% solution of D.D.T. in kerosene. It is well to spray again after a month's interval.

The chances that the building will be reinfested are not very great, for bugs live in structures (cracks in flooring, bedsteads, etc.) but not to any extent on persons or clothes. They may, however, be carried about occasionally on clothes and also in cracks in bundles, suitcases, and so forth.

The Chorda Tympani and a Persistent Unpleasant Taste

Q.—*Can a neurological lesion account for an unpleasant taste confined to the left side of the mouth and present for the last six months? The patient is a man of 60 with evidence of old left-sided mastoid infection.*

A.—It is unlikely that the unpleasant taste on the left side of the mouth in this patient results from a lesion of the chorda tympani. Loss of conduction in this nerve occurs in some cases of Bell's palsy, of chronic otitis media, and of acoustic nerve tumours, but only a few of these patients make any complaint of impairment of taste and they do not complain of a persistent unpleasant taste. With a lesion of the chorda tympani objective impairment of taste on the same side of the tongue can be demonstrated by testing with salt, sugar, quinine, and vinegar, and it would be worth testing taste sensation on both sides of the tongue in the patient.

Pain around the Achilles Tendon

Q.—*During the past 12 months I have seen several middle-aged patients, previously keen athletes, suffering from pain localized to about 1½ in. (3.8 cm.) above the insertion of the tendo Achillis. The condition is presumably due to a certain degree of degeneration, as it is the site at which the tendon is known to snap. Raising the heel, persistent short-wave diathermy, and transverse massage have had practically no effect. The other possible treatments appear to be plaster immobilization for six to eight weeks and slitting the tendon sheaths. Could you please supply any information on the efficacy of either of the latter two methods?*

A.—The condition described is not commonly met with in orthopaedic practice, and it is doubtful whether a degenerative lesion of the tendo calcaneus, with symptoms as described, is a definite entity. Pain in the region of the tendo calcaneus is usually due to a rupture of the tendon fibres, or to bursitis deep to the tendon or superficial to the heel just below the tendon insertion. Surprisingly, complete ruptures of the tendo calcaneus are often overlooked; but from the description given it seems unlikely that the cases described can be examples of rupture. Bursitis deep to the tendo calcaneus can give persistent pain of long duration. If it does not respond to physiotherapy, in the form of short-wave diathermy, it is worth while trying the effect of plaster immobilization, which is often successful if prolonged for about two months. Failing this, if the symptoms justify it, operative treatment is available. The operation should consist in excision of the bursa and fibro-fatty tissues deep to the tendon. The tendo calcaneus is surrounded by paratenon, but has no true sheath; it is therefore not subject to conditions such as teno-vaginitis that occur where tendons glide in sheaths.

Cortisone and Athletic Performance

Q.—*What is the effect of cortisone or A.C.T.H. on athletic performance? I am assuming a single large dose shortly before one of the longer running events—say, the mile (1.6 km.).*

A.—The working performance of adrenalectomized animals is increased by adrenal cortical extracts or by cortisone. But normal rats do not appear to have their muscular performance improved by either cortisone or A.C.T.H. No direct information appears to be available on the effects on athletic performance in man.

Rashes Accompanying Exudation of Serum

Q.—*What is the explanation of the rash which so frequently follows a lesion where serum flows—e.g., a burn or leg ulcer?*

A.—It is probable that many factors are involved, and in different cases different factors may predominate. The serum from a lesion may carry to the neighbouring skin (1) albumin which neutralizes the fatty acids which contribute to the self-sterilizing power of the skin; (2) bacteria, especially *Strep. pyogenes* and *Staph. aureus*; (3) enzymes and metabolites possibly harmful to the skin; and (4) moistness which lowers the death rate of bacteria, especially coliform bacilli, caused by drying. Contributory causes may arise from the lesion itself, which may alter the physiology of the surrounding skin and make it more liable to damage. An irritant local application may contribute to the rash, or the dressing may increase moistness by reducing evaporation, or cause friction.

The rash will often recover when the local lesion heals. If it needs special treatment the above factors should be investigated. A swab for bacteriological examination will indicate the colonizing flora and may aid a decision on the local management of the skin.

NOTES AND COMMENTS

Angular Stomatitis.—Dr. J. H. D. WEBSTER (Ruda, Sweden) writes: Your expert, replying to a query on angular stomatitis ("Any Questions?" November 1, p. 1006), replied giving only dental causes; this ignores the important fact that it is one sign of the Plummer-Vinson syndrome, the others being a smooth tongue and fragile flattened finger-nails. It is due to a hypochromic anaemia, is often (especially in Sweden, as Professor Ahlbom discovered many years ago) a precursor of post-cricoid malignant disease, and is cured by an assimilable iron preparation taken daily, and sometimes needed for many years to prevent relapses.

OUR EXPERT writes: In my reply it was indicated that nutritional causes were not being considered.

Correction.—The incidence of the more serious forms of mental illness accompanying childbirth discussed in Dr. R. E. Hemphill's article (December 6, p. 1232) was 1.4 per 1,000, not 1.4% as stated in the annotation (p. 1250).

"Any Questions?" Book: Second Series.—This is now available, price 7s. 6d. (postage 6d. extra), from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

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